

ESSENTIAL AND IMPORTANT GENES OF PSEUDOMONAS AERUGINOSA
AND THE USE THEREOF TO DESIGN OR IDENTIFY ANTIBACTERIAL
AGENTS

Cross Reference Related to Related Applications

[0001] This application relates to U.S. Provisional Serial No. 60/372,095, filed on April 15, 2002 and which is incorporated in their entirety by reference herein.

Field of Invention

[0002] The present invention relates to the identification of essential and important genes in *Pseudomonas aeruginosa*, and the use thereof in screening assays and diagnostic methods to identify, evaluate or design antibacterial agents useful for the treatment of *Pseudomonas* infections. Such agents are particularly useful in preventing and treating opportunistic infections in immunocompromised individuals and for treating and preventing pulmonary infections in patients having cystic fibrosis disease. Also disclosed is a Bayesian statistical model that may be utilized to increase the statistical confidence that any given gene identified using the disclosed methodology is essential.

Background of Invention

[0003] *Pseudomonas aeruginosa* is a versatile Gram-negative bacterium that is able to adapt to and thrive in many ecological niches, from water and soil to plant and animal tissues. The bacterium is capable of utilizing a wide range of organic compounds as food sources, thus giving it an exceptional ability to colonize ecological niches where nutrients are limited, such as soil, marshes and coastal marine habitats. Hardalo, C. & Edberg, S. C. *Pseudomonas aeruginosa*: assessment of risk from drinking water. *Crit. Rev. Microbiol.* 23, 47-75 (1997). It also forms biofilms on wet surfaces such as those of rocks and soil. Costerton, J. W., Stewart, P. S. & Greenberg, E. P. Bacterial biofilms: a common cause of persistent infections. *Science* 284, 1318-1322 (1999). Ahearn, D. G., Borazjani, R. N., Simmons, R. B. & Gabriel, M. M. Primary adhesion of *Pseudomonas aeruginosa* to inanimate surfaces including biomaterials. *Methods Enzymol.* 310, 551-557 (1999). Analysis of the *P. aeruginosa*

genome has identified genes involved in locomotion, attachment, transport and utilization of nutrients, antibiotic efflux, and two component and other regulatory systems involved in sensing and responding to environmental changes. Because its natural habitat is the soil, where it exposed to bacilli, actinomycetes and molds, it has developed resistance to a variety of their naturally-occurring antibiotics.

[0004] The emergence of *P. aeruginosa* as a major opportunistic human pathogen during the past century may be a consequence of its resistance to the antibiotics and disinfectants that eliminate other environmental bacteria. *P. aeruginosa* is now a significant source of bacteraemia in burn victims, urinary-tract infections in catheterized patients, and hospital-acquired pneumonia in patients on respirators. Bodey, G. P., Bolivar, R., Fainstein, V. & Jadeja, L. Infections caused by *Pseudomonas aeruginosa*. *Rev. Infect. Dis.* 5, 279-313 (1983). It is also the predominant cause of morbidity and mortality in cystic fibrosis patients, whose abnormal airway epithelia allow long-term colonization of the lungs by *P. aeruginosa*. Thus, people with cystic fibrosis, burn victims, individuals with cancer and AIDS, and patients requiring extensive stays in intensive care units are particularly at risk of disease resulting from *P. aeruginosa* infection. *P. aeruginosa* is also a cause of a variety of different disorders including septicemia, urinary tract infections, pneumonia and chronic lung infections, endocarditis, dermatitis, osteochondritis, ear and eye infections, bone and joint infections, gastrointestinal infections and skin and soft tissue infections, including wound infections, pyoderma and dermatitis.

[0005] Cystic fibrosis is one of the most common fatal genetic disorders in the United States, affecting about 30,000 individuals. A comparable number of people in Europe also have CF. It is most prevalent in the Caucasian population, occurring in one of every 3,300 live births. The gene involved in cystic fibrosis was identified in 1989 and codes for a protein called the cystic fibrosis transmembrane conductance regulator (CFTR). This protein, normally produced in a number of tissues throughout the body, regulates the movement of salt and water in and out of these cells. One hallmark of CF is the presence of a thick mucus secretion that clogs the bronchial tubes in the lungs and plugs the exit passages from pancreas and intestines, leading to loss of function of these organs and resulting in a predisposition toward chronic bacterial infections.

Pseudomonas aeruginosa, having a propensity to live in warm, wet environments, is a particular problem for CF patients, whose lungs typically become colonized (inhabited long-term) by *P. aeruginosa* before their 10th birthday. Although antibiotics can decrease the frequency and duration of these attacks, resistant bacteria are quick to develop and the bacteria are never completely eradicated from the lung. More effective antibiotics are necessary for improving lung function and quality of life for CF patients for extended time periods.

[0006] *Pseudomonas aeruginosa* is notorious for its resistance to antibiotics and is, therefore, a particularly dangerous and dreaded pathogen. Todor, K. 2000 *Pseudomonas aeruginosa*, University of Wisconsin-Madison, <http://www.bact.wisc.edu/microtextbook/disease/pseudomonas.html>, available on April 25, 2001. The permeability barrier afforded by its outer membrane LPS also contributes to its natural antibiotic resistance, as do the presence of two antibiotic resistance plasmids, both R-factors and RTFs, which are commonly transferred between cells by the bacterial processes of transduction and conjugation. Only a few antibiotics are effective against *Pseudomonas*, including tobramycin (TOBI; Chiron), fluoroquinolone, gentamicin and imipenem, and even these antibiotics are not effective against all strains.

[0007] *Pseudomonas aeruginosa* disease generally begins with some alteration or circumvention of normal host defenses and may involve several different virulence determinants. Todor, 2000, *supra*. The ultimate *Pseudomonas* infection may be seen as composed of three distinct stages: (1) bacterial attachment and colonization; (2) local invasion; (3) disseminated systemic disease. Particular bacterial determinants of virulence mediate each of these stages and are ultimately responsible for the characteristic syndromes that accompany the disease. For instance, *Pseudomonas* utilize fimbriae or pili to adhere to the epithelial cells, apparently via binding to specific galactose or mannose or sialic acid receptors on epithelial cells. Fimbrial adherence may be an important step in *Pseudomonas* keratitis and urinary tract infections, as well as infections of the respiratory tract. Mucoïd strains, which produce an a exopolysaccharide (alginate) have an additional or alternative adhesin which attaches to

the tracheobronchial mucin (N-acetylglucosamine). Therefore, mucoid strains of *P. aeruginosa* are commonly seen in lung infections.

[0008] The ability of *P. aeruginosa* to invade tissues depends upon its resistance to phagocytosis and the host immune defenses, and the extracellular enzymes and toxins that break down physical barriers and otherwise contribute to bacterial invasion. Todor, 2000, *supra*. For instance, *Pseudomonas* elastase cleaves collagen, IgG, IgA, and complement, and also lyses fibronectin to expose receptors for bacterial attachment on the mucosa of the lung. Alkaline protease interferes with fibrin formation and lyses fibrin. Together, elastase and alkaline protease destroy the ground substance of the cornea and other supporting structures composed of fibrin and elastin. Elastase and alkaline protease together are also reported to cause the inactivation of gamma Interferon (IFN) and Tumor Necrosis Factor (TNF).

[0009] *P. aeruginosa* produces three other soluble proteins involved in invasion, including a cytotoxin (MW 25,000) and two hemolysins. Todor, 2000, *supra*. The cytotoxin is a pore-forming protein originally named leukocidin because of its effect on neutrophils, but it appears to be cytotoxic for most eukaryotic cells. Of the two hemolysins, one is a phospholipase and the other is a lecithinase. They appear to act synergistically to break down lipids and lecithin. The cytotoxin and hemolysins contribute to invasion through their cytotoxic effects on eukaryotic cells.

[0010] *Pseudomonas aeruginosa* also produces two extracellular protein toxins, Exoenzyme S and Exotoxin A. Exoenzyme S may act to impair the function of phagocytic cells in the bloodstream and internal organs to prepare for invasion by *P. aeruginosa*, and is typically produced by bacteria growing in burned tissue. Exotoxin A is partially identical to diphtheria toxin, and exhibits a necrotizing activity at the site of bacterial colonization and is thereby thought to contribute to the colonization process. Indirect evidence involving the role of exotoxin A in disease is seen in the increased chance of survival in patients with *Pseudomonas* septicemia that is correlated with the titer of anti-exotoxin A antibodies in the serum.

[0011] While therapeutic measures aimed at any of the above virulence factors may help to slow the progression of an infection and may be useful in combined therapeutic

regimens, given the variety of virulence factors of *P. aeruginosa*, antibacterial agents that inhibit growing bacteria by interacting with essential genes and essential gene products are necessary. Although, this is not to say that genes encoding virulence factors would not be essential to survival in particular niches or environments, emphasizing the importance of screening for gene essentiality in various pathogenic environments. See, e.g., Coulter et al., 1998, *Staphylococcus aureus* genetic loci impacting growth and survival in multiple infection environments, Mol. Microbiol. 30(2): 393-404. However, as *P. aeruginosa* becomes more and more resistant to existing antibacterial agents, new compounds are required.

[0012] Indeed, reports of bacterial strains resistant to the most powerful known antibiotics are becoming more common, signaling that new antibiotics are needed for all bacteria, not only *P. aeruginosa*. For instance, the United States Center for Disease Control recently announced that one of the most powerful known antibiotics, vancomycin, was unable to treat an infection of *Staphylococcus aureus* (staph), an organism commonly found in the environment and responsible for many nosocomial infections. If this trend continues, some have warned that we could return to a time when a common bacterial infection is a life threatening matter. See Zyskind et al., WO 00/44906, published August 3, 2000.

[0013] Historically, however, the identification of new antibacterial drugs has been painstaking and laborious with no guarantee of success. Traditional methods involve blindly and randomly testing potential drug candidate molecules, with the hopes that one might be effective. Today, the average cost to discover and develop a new drug is nearly \$500 million, and the average time is 15 years from laboratory to patient. New identification and screening methods that shorten and improve this process are much needed.

[0014] A newly emerging technique for identifying new antibacterial agents is to first identify gene sequences and proteins required for the proliferation of bacteria, or "essential" genes and proteins, and then conduct a biochemical and structural analysis of that target gene or protein in order to derive compounds that interact with the target. Such methodology employs molecular modeling techniques, combinatorial chemistry

and other means to design candidate drugs, and offers a more directed alternative to merely screening random compounds with the hope that one might be suitable for a particular bacterium.

[0015] Nevertheless, even this preferred approach presents obstacles including the identification of essential genes and proteins, and the design of new assays for the genes thus identified in order to efficiently screen candidate compounds. Several groups have proposed systems for the identification of essential genes. For instance, Zyskind and colleagues propose a method of identifying essential genes in *Escherichia coli* by subcloning a library of *E. coli* nucleic acid sequences into an inducible expression vector, introducing the vectors into a population of *E. coli* cells, isolating those vectors that, upon activation and expression, negatively impact the growth of the *E. coli* cell, and characterizing the nucleic acid sequences and open reading frames contained on the subclones identified. See WO 00/44906, herein incorporated by reference. The disadvantage of this method is that the overexpression of nonessential genes can also negatively impact the cell, particularly the overexpression of membrane proteins and sugar transport proteins that are not necessary for growth where alternative carbon sources exist. Such proteins typically become trapped in membrane export systems when the cell is overloaded, and would be identified by this methodology. See Muller, FEMS Microbiol. Lett. 1999 Jul 1;176(1):219-27.

[0016] Another group proposes the identification of growth conditional mutants, and more specifically temperature sensitive (ts) mutants, as a means to identify essential genes in *Staphylococcus aureus*. See Benton et al., U.S. Patent 6,037,123, issued March 14, 2000, herein incorporated by reference. Each gene is identified by isolating recombinant bacteria derived from growth conditional mutant strains, i.e., following introduction of a vector containing a library of nucleic acid sequences, which would grow under non-permissive conditions but which were not revertants. These recombinant bacteria were found to contain DNA inserts that encoded wild type gene products that replaced the function of the mutated gene under non-permissive growth conditions. By this method, Benton and colleagues were able to identify 38 loci on the *S. aureus* chromosome, each consisting of at least one essential gene.

[0017] The disadvantages of this method are first, the chemical employed to induce mutagenesis (diethyl sulfate, DES) is capable of causing several mutations in the same cell, thereby complicating interpretation of the results. Second, the method is particularly labor intensive in that one must painstakingly analyze replica plates of individual colonies grown at permissive and non-permissive temperatures, where replica plates include both mutant and non-mutant cells. Thus, employing the appropriate level of mutagen to achieve a balance between minimizing the number of non-mutant colonies one must screen in order to identify one mutant, while at the same time avoiding multiple mutations in the same cell, may be an arduous task.

[0018] Another group has proposed a transposon mutagenesis system for identifying essential genes called "GAMBIT" ("genomic analysis and mapping by *in vitro* transposition"), and has used the system to identify essential genes first in the gram positive bacteria *Haemophilus influenzae* and *Streptococcus pneumoniae*, and more recently in *Pseudomonas aeruginosa*. See Akerley et al., Systematic identification of essential genes by *In vitro mariner* mutagenesis, Proc. Natl. Acad. Sci USA 95(15): 8927-32; Wong and Mekalanos, 2000, Proc. Natl. Acad. Sci. USA 97(18): 10191-96; and Mekalanos et al., U.S. Patent No. 6,207,384, issued March 27, 2001, herein incorporated by reference. GAMBIT involves first isolating and purifying specific genomic segments of approximately 10 kilobases using extended-length PCR, and creating a high density transposon insertion map of the isolated region using *Himar I* transposon mutagenesis. The transposon insertions are then transferred to the chromosome following transformation of the bacteria with the transposon containing vectors, and selection for the antibiotic resistance marker on the transposon. The position of each transposon insertion with respect to a given PCR primer is then determined by genetic footprinting, i.e., by amplifying sub-PCR products using one of the original PCR primers and a primer that recognizes an internal site in the *Himar I* transposon. By analyzing the length of PCR fragments thus identified, it is possible to identify regions that are devoid of transposon insertions, thereby signaling regions that might contain essential genes.

[0019] While the GAMBIT method is a good technique for looking at a small region of the genome for essential genes, it would be extremely labor intensive to use this

method for analyzing the entire genome. This is particularly true for *P. aeruginosa*, whose genome (~6 megabases) is about 70% greater in size than the *H. influenzae* genome (~1.8 megabases). Furthermore, GAMBIT would not be readily applicable to use in organisms that are less recombinogenic than *H. influenzae*. Indeed, while the *H. influenzae* genome contains about 1700 protein coding genes, *P. aeruginosa* contains about 5570. According to U.S. Patent 6,207,384, one would need to clone and mutagenize the 6 million base pair genome of *P. aeruginosa* in 10,000 base pair fragments, isolating and characterizing 400-800 mutants per 10,000 base pair fragment. Generating 6×10^5 mutants and characterizing them via PCR on gels would require a significant investment of labor, materials and time.

[0020] Another group at Abbott Laboratories has proposed a genome scanning method for identification of putative essential genes in *H. influenzae*, whereby random transposon insertions are mapped and analyzed to identify open reading frames containing no insertion in order to identify putative essential genes. Reich et al., 1999, Genome Scanning in *Haemophilus influenzae* for Identification of Essential Genes, J. Bacteriol. 181(16): 4961-68. However, even though transposon insertions were isolated that spanned the whole genome, the authors employed a genomic footprinting technique similar to that used in GAMBIT to map insertions in a short contiguous region of the chromosome. The method further employs the methods of mutation exclusion and zero time analysis in order to monitor the fate of individual insertions after transformation in growing culture, which looks at individual insertions on a case-by-case basis. Again, such techniques would be extremely labor-intensive for the *P. aeruginosa* genome, which is 70% larger than the genome of *H. influenzae*.

[0021] Wong and Mekalanos also proposed identifying essential genes in *P. aeruginosa* by starting with the knowledge of three essential genes in *H. influenzae* and using genetic footprint analysis to determine if the homologues of these genes are essential in *P. aeruginosa*. Of three homologues tested, only one was unable to accommodate a transposon insertion. See Wong and Mekalanos, *supra*. Such results underscore the fact that a gene that is shown to be essential in one species will not necessarily be essential in another, given that some gene products may fulfill different functional roles in different species. Furthermore, given the larger coding capacity of

the *P. aeruginosa* genome relative to that of other bacteria, it would not be surprising for *P. aeruginosa* to possess an increase in redundant gene functions, thereby decreasing the actual number of essential genes, and making them more difficult to identify.

[0022] Another method is entitled Transposon Mediated Differential Hybridisation (TMDH), which is disclosed in WO 01/07651, herein incorporated by reference. This method entails (i) providing a library of transposon mutants of the target organism; (ii) isolating polynucleotide sequences from the library which flank inserted transposons; (iii) hybridising said polynucleotide sequences with a polynucleotide library from said organism; and (iv) identifying a polynucleotide in the polynucleotide library to which said polynucleotide sequences do not hybridise in order to identify an essential gene of the organism. However, the problem with this methodology is that it has a high propensity to lead to false positives, and many essential genes will be missed. Furthermore, the method does not yield any detailed information regarding the loci disrupted by transposons, or whether they were hit more than once.

[0023] Thus, there is a great need for more efficient methods to identify essential genes, particularly in *P. aeruginosa*, so that new antibacterial agents may be designed therefrom for use in treatment of *P. aeruginosa* infections.

Summary of Invention

[0024] The present inventors have devised a database of potential essential or otherwise important genes in *P. aeruginosa*, which may be used to verify essentiality and design antibacterial agents active against the targets thus identified. In particular, the inventors have isolated and mapped a library of at least about 5,000 to at least about 14,000 transposon insertions in the genome of *P. aeruginosa*, and more preferably a library of at least about 8000 to at least about 14,000 transposon insertions, and even more preferably a library of at least about 10,000 to at least about 14,000 transposon insertions, using the recently published *P. aeruginosa* gene sequence. The map thus generated was used to form a database of approximately 1500 to 3000 open reading frames, or more preferably about 1500 to 2000 open reading frames, for which no transposon insertions could be obtained, each of which possibly represents an essential

gene required for growth and proliferation of *P. aeruginosa* on rich media, or an important gene, the mutation of which results in an attenuated growth mutant. Also disclosed is a Bayesian statistical model that may be utilized to increase the statistical confidence that any given gene identified using the disclosed methodology is essential.

[0025] Thus, one aspect of the invention is a database of putative essential or otherwise important genes, defined by the absence of transposon insertions in those genes in a High Throughput Transposon Insertion Map (HTTIM) database comprising about 10,000 to about 14,000 transposon insertions in the genome of *Pseudomonas aeruginosa*. Minimally, such a database comprises approximately 1800 open reading frames (ORFs), each of which may be further tested for essentiality using a variety of tests disclosed herein. However, predictions of essentiality or importance may be bolstered based on length of the ORF and predicted function and other statistical factors, thereby providing for more narrow databases of putative essential genes. Thus, the invention also includes databases that are more narrow and comprise only those genes for which essentiality or importance may be predicted with at least an 80% confidence level, and include at least about 850 to about 875 genes. The invention also includes databases assigned a confidence level of about 85% and including at least about 675 to about 700 genes. The invention further includes databases assigned a confidence level of about 90% including at least about 475 to about 500 genes. Further, the invention includes databases assigned a confidence level of about 95% and including at least about 200 to 250 genes.

[0026] The transposon insertion map and database of putative essential or otherwise important open reading frames (ORFs) obtained may be used to confirm the essentiality or importance of genes, for example by integration knock outs in the presence of chromosomal complementation or by integration and activation of a regulatable promoter. An "essential" gene is one that cannot be "knocked out," i.e. for which null mutants having complete absence of the gene product are not viable. This does not mean, however, that such genes could not tolerate point mutations or truncations that preserve sufficient gene product function so as to enable cell growth and survival. Essential genes are to be distinguished from "important" genes, which are also included in the present invention, in that a "knock out" of an important gene does not lead to cell

death but rather results in an attenuated growth mutant. Such genes may be included in the database of open reading frames not hit by random transposon mutagenesis as described herein, because attenuated growth colonies may be significantly smaller than the average *P. aeruginosa* colony and may have been overlooked when transposon insertion mutants were picked to generate the high throughput transposon insertion database (HTTIM).

[0027] Nevertheless, important gene products may interact with or regulate other genes, gene products or cellular processes that are essential, thereby making such gene products appropriate targets for drug design. Moreover, most drugs don't effectively kill all the pathogenic bacteria in the body; rather, they kill or growth attenuate a portion of the bacteria, empowering the immune system to target the remainder. Hence, important genes that, when targeted with an antibacterial agent, result in attenuated growth, are also targets for the antibacterial drugs of the present invention.

[0028] The invention also includes a database of attenuated growth mutants identified from the HTTIM transposon database. The genes marked by such mutations are of the same class of importance as the "important" genes identified in the no-hit database of genes, except that the growth attenuated nature of such transposon mutants was discovered at the transposon mutagenesis stage, rather than at the stage where essentiality is tested via targeted knock out. Thus, genes that when mutated confer attenuated growth may be identified from two sources: (1) from the library of open reading frames that did not receive a transposon insertion during HTTIM but were subsequently identified as an important gene when essentiality was tested via knock out and/or promoter swap strategies, and (2) from the HTTIM database itself when in the process of accumulating transposon insertion mutants it was observed that a particular insertion conferred an attenuated growth phenotype.

[0029] Such attenuated mutants grow more slowly than wild type, and may grow more slowly due to reduced expression of an essential gene, i.e., transposon is in gene that regulates expression of an essential gene, or due to expression of a truncated form of an essential gene, i.e., transposon is in the essential gene itself and leads to expression of a truncated mRNA. For example, mutants that show a higher drug

susceptibility could be the result of insertions in a gene that potentiates resistance, such as an efflux pump, or due to reduced expression of essential genes involved in the mechanism of action of the drug. Expression of mutated forms of essential and important genes may make the cell more susceptible to compounds that inhibit that particular gene or gene product, and may allow the identification of antibacterial agents with greater sensitivity. Furthermore, screening in whole cells overcomes the potential problems of uptake and efflux that are sometimes an issue for compounds identified via enzyme-based assays.

[0030] The essential and important genes of the invention may be used to design, screen for and evaluate potential antibacterial agents for the purpose of developing new treatments for *P. aeruginosa* infection. Antibacterial agents identified according to the invention may have activity against the gene or against the corresponding gene product or metabolic pathways requiring the gene product. For instance, antibacterial agents according to the invention may include antisense nucleic acids or regulatory proteins that bind to open reading frames, to upstream polar sequences or to promoters that drive expression of the genes encoded by such open reading frames. Active agents according to the invention may also include antibodies or proteins that bind to proteins encoded by open reading frames, or to transcriptional or translational regulators of such genes or proteins, or to binding partners of such proteins. Agents may also be chemical compounds designed following molecular modeling of essential gene products according to the invention, or mutant proteins designed therefrom that compete with the essential wild type protein for reactive cell components or for interacting nutrients, as well as agents from random chemical.

[0031] The present invention therefore includes methods and assays for identifying antibacterial agents having specificity for the essential or important open reading frames identified, or to genes and proteins that interact with such open reading frames or the products encoded thereby. Once essential and important open reading frames are identified, antibacterial agents may be identified using the assays and methods described herein, or by any suitable assay. Such assays may vary depending on the function delineated for each essential locus, as would be apparent to those of skill in the art. For instance, enzyme assays may be designed based on the predicted function of

essential and important genes in order to define classes of inhibitors to be tested. Also, random chemical libraries may be screened for activity against the isolated genes or gene products. Cell lines may be designed or isolated that demonstrate reduced expression of essential genes, thereby providing a sensitive screening tool for inhibitors that effect the activity of that gene or gene product as it functions in the cell. Such cell lines may be devised from cells having transposon insertions that lead to attenuated growth, or may be constructed by the promoter swap techniques described herein, by using a regulatable promoter that can be used to increase gene expression, allowing for confirmation of target specificity. Here, the minimal inhibitory concentration of the inhibitor is directly related to the expression level of the target gene, such that under low expression, an attenuated growth cell is more susceptible to an inhibitor than the wild type strain, and as you raise the expression level, the minimum inhibitory concentration (MIC) increases. The MIC shift will be consistent when the inhibitor acts on the regulated target.

[0032] Active agents and compounds can be formulated into pharmaceutical compounds and compositions, effective for treating and preventing *Pseudomonas* infections in accordance with the methods of the invention. Such therapy will be particularly useful in the hospital setting for preventing and treating nosocomial infections, and for administering to cystic fibrosis patients to improve lung function and quality of life. Depending on the activity of the essential or important gene targeted, such agents could also be useful in treating all types of *Pseudomonas* infections ranging from bacteraemia and septicemia, urinary-tract infections, pneumonia and chronic lung infections, burn infections, cancer, AIDS, endocarditis, dermatitis, osteochondritis, ear and eye infections, bone and joint infections, gastrointestinal infections and skin and soft tissue infections, including wound infections, pyoderma and dermatitis. Further, the invention provides pharmaceutical compositions appropriate for use in methods of treating bacterial infections described above.

Brief Description of the Drawings

[0033] Figure 1. Depiction of a single crossover recombination event resulting in integration of a plasmid into the bacterial chromosome. Isolation of such recombinants indicates that the targeted gene is not essential.

[0034] Figure 2. Single crossover and integration of a plasmid resulting in the replacement of a wild type promoter with a regulatable promoter.

[0035] Figure 3. Depiction of the 'promoter swap' strategy, using transformation of pBEM10 into *P. aeruginosa* in order to replace the *lpxC* promoter with the arabinose *araBAD* promoter, thereby allowing modulation of its *lpxC* expression by the use of a simple sugar, arabinose.

[0036] Figure 4. Graph showing the susceptibility or non-susceptibility of various *E. coli* and *P. aeruginosa* strains to the inhibitor L161,240.

[0037] Figure 5. Graph depicting the effect of tetracycline and L161,240 on the growth of *P. aeruginosa* strain PA01 with and without polymixin permeabilization.

[0038] Figure 6. Sensitivity of various *E. coli* and *P. aeruginosa* strains to inhibitor L161,240 following promoter swap and transformation with vector expressing *E. coli lpxC* or *P. aeruginosa lpxC*. *E. coli* "swaps" refer to *P. aeruginosa* containing a vector comprising *E. coli lpxC*, and "PA swaps" refer to *P. aeruginosa* containing a vector comprising *P. aeruginosa lpxC*.

[0039] Figure 7. Graph illustrating ORF coverage by Tn5 achieved in High-Throughput Transposon Insertion Mapping (HTTIM), wherein 30% of the genes in the genome are candidate essential genes where ORF size is not taken into account in predicting essentiality.

[0040] Figure 8. Graph depicting the probability of identifying an essential gene given no transposon insertion, as a function of gene size.

[0041] Figure 9. A circular map of the *P. aeruginosa* genome showing distribution of transposon insertion sites constituting a HTTIM of the invention, and demonstrating the

random nature of the transposon employed. The length of the bars radiating outward from the center of the circular map reflect the number of transposon insertions per non-overlapping kilobase.

[0042] Figure 10. Histogram depicting the number of ORFs in the *P. aeruginosa* genome of (a) up to 4000 base pairs and (b) from 4000 up to 16884 base pairs.

[0043] Figure 11. Graph showing likelihood and accumulative likelihood gains.

[0044] Figure 12. Trajectory of the algorithm projected in a subspace spanned by two gene sizes. The x-axis represents genes of sizes 151-160 DNA base-pairs and y-axis represents genes of sizes 171- 180 DNA base-pairs. Here $n=(2,1)$ and $M=(7,9)$. The median gene size of each group is used as the gene size. At iteration number 66, the likelihood gain is maximum in the direction of increasing the number of nonessential genes by one for genes with size 171-180 DNA base-pairs. At iteration number 443, the largest likelihood gain is obtained in the direction of increasing one nonessential genes for genes of sizes 151-160 DNA base pair. At any point, moving backwards has a negative likelihood gain.

[0045] Figure 13. More trajectories of the searching algorithm projected in different subspaces.

[0046] Figure 14. Plot of likelihood for different initial values.

[0047] Figure 15. Trajectories of the algorithm with different starting values projected in the subspace spanned by two gene sizes: 1101-1150 DNA base-pairs for X-axis and 921-930 DNA base-pairs for y-axis.

[0048] Figure 16. Top: (A) The top line is \bar{M} , number of genes, the bottom line is \bar{n} , the number of genes with at least one observed insertion; the line in the middle is \bar{N} , the number of estimated nonessential genes. For demonstration purpose, a cubic spline smooth is applied to the data. Bottom: Histogram of resamples of $\hat{\gamma}$ (B) and $\hat{\lambda}$ (C).

[0049] Figure 17. Plot of \hat{N}_i/M_i . The dotted line is the value of \hat{N}_i/M_i , and the solid line is a moving average smooth.

[0050] The essential and important open reading frames identified in the present invention were originally part of a library of putative nucleic acid sequences generated from *P. aeruginosa* strains PA01 and PAK. See Table 1. Nevertheless, it is expected that the genes identified will also be essential or important in related *P. aeruginosa* strains as well as other *Pseudomonas* species, given the low sequence diversity that exists between *P. aeruginosa* strains of widely diverse environments and the pronounced structural and functional homology of gene products. See, e.g., Spangenberg et al., 1998, Structural and functional implications of sequence diversity of *Pseudomonas aeruginosa* genes *oriT*, *ampC* and *fliC*, Electrophoresis 19(4): 545-50; Ruimy et al., 2001, Genetic diversity of *Pseudomonas aeruginosa* strains isolated from ventilated patients with nosocomial pneumonia, cancer patients, bacteremia, and environmental water, Infect. Immun. 69(1): 584-8. For instance, comparative sequencing of several *P. aeruginosa* genes from several environmental and clinical isolates revealed the sequence diversity to be about one order of magnitude lower than in comparable housekeeping genes from *Salmonella*. See Kiewitz and Tummeler, 2000, Sequence diversity of *Pseudomonas aeruginosa*: impact on population structure and genome evolution, J. Bacteriol. 182(11): 3125-35. Thus, it is expected that agents identified as antibacterial based on their interaction with genes or gene products of *P. aeruginosa* PA01 or PAK will be broadly applicable as antibacterial agents against a variety of *Pseudomonas* species as well as other bacteria including but not limited to *Escherichia*, *Hemophilus*, *Vibrio*, *Borrelia*, *Enterococcus*, *Heliobacter*, *Legionella*, *Mycobacterium*, *Mycoplasma*, *Neisseria*, *Staphylococcus*, *Streptococcus*, etc.

[0051] Thus, the present invention encompasses an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide having at least 80% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1. More preferably, the present invention encompasses an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide having at least about 85 to 90% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open

reading frames (ORFs) listed in Table 1. Even more preferably, the present invention encompasses an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide having at least about 90 to about 95% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1.

[0052] In particular, the invention encompasses isolated nucleic acid molecules comprising nucleic acid sequences encoding polypeptides having at least 80% sequence identity, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential or important nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein essentiality or importance of said nucleic acid sequence is determined by integration knock-out coupled with extra-chromosomal complementation. Likewise, the invention encompasses isolated nucleic acid molecules comprising nucleic acid sequences encoding polypeptides having at least 80% sequence identity, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein essentiality or importance of said nucleic acid sequence is determined by integration of a regulatable promoter into the gene, or via any other suitable method.

[0053] In one embodiment, the polynucleotides of the invention are recombinant. Recombinant polynucleotides of the invention include proteins of genomic, cDNA, semisynthetic, or synthetic origin, which, by virtue of its origin or manipulation (1) is not associated with all or a portion of a polynucleotide with which it is associated in nature; (2) is linked to a polynucleotide other than that to which it is linked in nature; or (3) does not occur in nature.

[0054] Given that the library of nucleic acid sequences encompassed in Table 1 provides an unprecedented tool useful for the identification of essential and otherwise important genes in *Pseudomonas* and the construction and isolation of attenuated mutants, the present invention includes a library of nucleic acid sequences consisting essentially of nucleic acid sequences having at least 70% sequence identity, or more

preferably at least about 80 to 90 to 95% identity, to a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein said library of nucleic acid sequences is employed to identify essential or otherwise important genes or to construct or isolate attenuated mutants in *Pseudomonas*.

[0055] Also encompassed in the invention is a map of at least about 10,000 to about 14,000 transposon insertions in the genome of *Pseudomonas aeruginosa* (High-Throughput Transposon Insertion Database or HTTIM), wherein said map is useful for identifying genes that are essential or important for survival of said *Pseudomonas aeruginosa*, i.e., by permitting the generation of a database of open reading frames that do not contain a transposon insertion. Figure 9 contains a circular map of the *P. aeruginosa* genome depicting 12,000 to 13,000 transposon insertion sites constituting a HTTIM of the invention, and demonstrates the random nature of the transposon employed. The length of the bars radiating outward from the center of the circular map reflect the number of transposon insertions per non-overlapping kilobase. Table 3 contains a list of 13,515 specific Tn5 transposon insertion sites generated in either PAK or PA01, with the 473 mutants 12516-13043 being identified as attenuated for growth.

[0056] Thus, the databases and libraries disclosed herein may be used to formulate useful subsets of these libraries and databases. Accordingly, the invention includes subsets of the databases and libraries disclosed. For instance, mutants 12516-13043 are identified as attenuated for growth and as such, the genes in this subset could be useful drug targets. Accordingly, this group of 473 mutants from the HTTIM database of 13,515 transposon hits provides a useful subset database for comparing homologies with essential genes of other organisms, for computer modeling of potential antibacterial agents, etc. A particularly useful database subset is one containing essential genes from *P. aeruginosa* that are also identified as essential in other Gram negative or Gram positive bacteria. Indeed, genes that have essential homologs in other bugs are likely to provide useful targets for broad spectrum antibacterial agents, i.e., agents that have broad spectrum activity as an antibacterial agent. Genes in the putative essential or important gene database have already been identified via BLAST

or other database analyses, and constitute an exemplary subset database of the present invention. See Table 4.

[0057] Further, the databases and subset databases of the present invention may also be used as comparative tools with other like databases or database subsets to identify broad spectrum. For instance, particularly envisioned is an embodiment wherein the database of putative essential and important genes identified in *P. aeruginosa* is cross-referenced with a similar database formed from *S. aureus*, wherein homologues present in both databases signal a potential target for a broad spectrum antibacterial agent. Cross-referencing between *P. aeruginosa* and *S. aureus* in particular will identify antibacterial targets for identifying broad spectrum antibiotics active against both Gram negative and Gram positive bacteria. However, databases derived from any bacteria could be employed in such comparisons, as well as databases formed from yeast, fungi, mycoplasma, and other potential pathogens.

[0058] Also encompassed in the invention is the use of essential and important genes and the corresponding proteins expressed thereto in the design of vaccines for eliciting prophylactic or therapeutic immune responses against *Pseudomonas aeruginosa*.

[0059] Such vaccines will typically comprise a *Pseudomonas aeruginosa* protein antigen or fragment or variant thereof encoded by an essential gene. Additionally, such antigens will preferably be a protein expressed on the surface of the bacteria.

[0060] Such vaccines will typically comprise a *Pseudomonas aeruginosa* protein antigen or fragment or derivative thereof encoded by an essential or important gene. Preferably, the protein antigen expressed from a recombinant polynucleotide.

[0061] Where the invention is directed to a fragment of a protein encoded by an essential or important gene, said fragment is preferably at least 8 to 12 amino acids long, and even more preferably at least about 20 to 30 amino acids long. Preferably, the fragment comprises either a B cell or a T cell epitope.

[0062] Where the invention is directed to a derivative of a protein encoded by an essential or important gene, said derivative contains one or more amino acid substitutions, additions or deletions. Preferably, the amino acid substitutions are

conservative amino acid replacements. Conservative amino acid replacements are those that take place within a family of amino acids that are related in their side chains. Genetically encoded amino acids are generally divided into four families: (1) acidic = aspartate, glutamate; (2) basic = lysine, arginine, histidine; (3) non-polar = alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar = glycine, asparagine, glutamine, cystine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. For example, it is reasonably predictable that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with glutamate, a threonine with a serine, or a similar conservative replacement of an amino acid with a structurally related amino acid will not have a major effect on the biological activity. Polypeptide molecules having substantially the same amino acid sequence as the protein by possessing minor amino acid substitutions that do not substantially affect the functional aspects are encompassed within the scope of derivatives of the proteins of the invention.

[0063] The polypeptide fragment or derivative is preferably immunologically identifiable with the polypeptide encoded by the essential or important gene. The polypeptide fragment or derivative is preferably immunogenic and is able to cause a humoral and/or cellular immune response, either alone or when linked to a carrier, in the presence or absence of an adjuvant. The polypeptide fragment or derivative may be fused to or incorporated into another polypeptide sequence. This other polypeptide sequence may include one or more other proteins, fragments or derivatives thereof encoded by an essential or important gene. The other polypeptide sequence may also include a polypeptide sequence which allows for presentation of the polypeptide fragment or derivative.

[0064] Accordingly, the present invention encompasses an isolated polypeptide and fragments and derivatives thereof, wherein said polypeptide has at least 80% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1. More preferably, the present invention encompasses an isolated polypeptide and fragments and derivatives thereof, wherein said polypeptide has at least about 85 to 90% sequence identity to a polypeptide encoded by a nucleic acid sequence selected

from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1. Even more preferably, the present invention encompasses an isolated polypeptide and fragments and derivatives thereof, wherein said polypeptide has at least about 90% to about 95% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1.

[0065] In particular, the invention encompasses isolated polypeptides and fragments and derivatives thereof, wherein said polypeptides have at least 80% sequence identity, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential or important nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein the essentiality or importance of said nucleic acid sequence is determined by integration knock-out couple with extra-chromosomal complementation. Likewise, the invention encompasses isolated polypeptides and fragments and derivatives thereof, wherein said polypeptides have at least 80% sequence identify, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein essentiality or importance of said nucleic acid sequence is determined by integration of a regulatable promoter into the gene, or via any other suitable method.

[0066] Also encompassed in the invention are therapeutic and prophylactic vaccines that comprise ligands that specifically bind antigens encoded by essential or important genes identified according to the invention, for use in, for instance, passive immunization. Preferred ligands are antibodies and antibody fragments that specifically bind the antigen encoded by the essential gene. Such antibodies may be polyclonal or monoclonal. Types of antibodies and antibody fragments include by way of examples murine antibodies, chimeric, antibodies, humanized antibodies, Fab fragments, Fab₂ fragments and human antibodies and scFv's. Methods for producing antibodies and antibody fragments by recombinant and non-recombinant methods are well known to those skilled in the art. In some embodiments the antigen used in such

passive immunization may be attached to a cytotoxic moiety, e.g., a radionuclide or other agent that is cytotoxic against the bacteria.

[0067] Further encompassed within the scope of the invention are cells or viral vectors that express on their surface a *Pseudomonas aeruginosa* essential gene, fragment or variant identified according to the invention.

[0068] In the case of prophylactic vaccines, the vaccine will comprise an immunogenic composition comprising a prophylactically effective amount of an antigen, antibody, cells or vector expressing an antigen encoded by an essential or important gene and will be formulated such that upon administration it elicits a protective immune response. In the case of therapeutic vaccines, the vaccine will comprise an immunogenic composition comprising a therapeutically effective amount of an antigen, antibody, cells or vectors expressing an antigen encoded by an essential or important gene and will be formulated such that upon administration it elicits a therapeutic immune response. Dosage effective amounts of prophylactic and therapeutic vaccines will be determined by known methods and will typically vary from about 0.00001 g/kg body weight to about 5-10 g/kg body weight.

[0069] The immunogenic compositions of the invention can be administered by known methods, i.e., mucosally or parenterally.

[0070] Suitable routes of mucosal administration include oral, intranasal (IN), intragastric, pulmonary, intestinal, rectal, ocular, and vaginal routes. Preferably, mucosal administration is oral or intranasal.

[0071] Where mucosal administration is used, the immunogenic composition is preferably adapted for mucosal administration. For instance, where the composition is administered orally, it may be in the form of tablets or capsules (optionally enteric-coated), liquid, transgenic plants, etc. Where the composition is administered intranasally, it may be in the form of a nasal spray, nasal drops, gel or powder. Where the antigen composition is adapted for mucosal administration, it may further be formulated such that the antigen remains stable, for instance by the use of carriers and excipients.

[0072] The immunogenic compositions of the invention can further comprise a mucosal adjuvant. Mucosal adjuvants suitable for use in the invention include (a) *E. coli* heat-labile enterotoxin ("LT"), or detoxified mutants thereof, such as the K63 or R72 mutants; (B) cholera toxin ("CT"), or detoxified mutants thereof; or (C) microparticles (i.e., a particle of ~100nm to ~150µm in diameter, more preferably ~200nm to ~30µm in diameter, and most preferably ~500nm to ~10µm in diameter) formed from materials that are biodegradable and non-toxic (e.g. a poly(α-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone *etc.*); (D) a polyoxyethylene ether or a polyoxyethylene ester (*see* International patent application WO 99/52549); (E) a polyoxyethylene sorbitan ester surfactant in combination with an octoxynol (*see* International patent application WO 01/21207) or a polyoxyethylene alkyl ether or ester surfactant in combination with at least one additional non-ionic surfactant such as an octoxynol (*see* International patent application WO 01/21152); (F) chitosan (e.g. International patent application WO 99/27960) and (G) an immunostimulatory oligonucleotide (e.g. a CpG oligonucleotide) and a saponin (*see* International patent application WO 00/62800). Other mucosal adjuvants are also available (e.g. see chapter 7 of *Vaccine design: the subunit and adjuvant approach*, eds. Powell & Newman, Plenum Press 1995 (ISBN 0-306-44867-X)).

[0073] Mutants of LT are preferred mucosal adjuvants, in particular the "K63" and "R72" mutants (e.g. see International patent application WO 98/18928), as these result in an enhanced immune response.

[0073] Microparticles are also preferred mucosal adjuvants. These are preferably derived from a poly(α-hydroxy acid), in particular, from a poly(lactide) ("PLA"), a copolymer of D,L-lactide and glycolide or glycolic acid, such as a poly(D,L-lactide-co-glycolide) ("PLG" or "PLGA"), or a copolymer of D,L-lactide and caprolactone. The microparticles may be derived from any of various polymeric starting materials which have a variety of molecular weights and, in the case of the copolymers such as PLG, a variety of lactide:glycolide ratios, the selection of which will be largely a matter of choice, depending in part on the coadministered antigen.

[0074] Antigen may be entrapped within the microparticles, or may be adsorbed to them.

[0075] Entrapment within PLG microparticles is preferred. PLG microparticles are discussed in further detail in Morris et al., (1994), *Vaccine*, 12:5 – 11, in chapter 13 of *Mucosal Vaccines*, eds. Kiyono et al., Academic Press 1996 (ISBN 012410587), and in chapters 16 & 18 of *Vaccine design: the subunit and adjuvant approach*, eds. Powell & Newman, Plenum Press 1995 (ISBN 0-306-44867-X).

[0076] LT mutants may advantageously be used in combination with microparticle-entrapped antigen, resulting in significantly enhanced immune responses.

[0077] Suitable routes of parenteral administration include intramuscular (IM), subcutaneous, intravenous, intraperitoneal, intradermal, transcutaneous, and transdermal (*see e.g.*, International patent application WO 98/20734) routes, as well as delivery to the interstitial space of a tissue.

[0078] The immunogenic compositions of the invention may be adapted for parenteral administration (*e.g.*, in the form of an injectable, which will typically be sterile and pyrogen-free).

[0079] The immunogenic composition may further comprise a parenteral adjuvant. Parenteral adjuvants suitable for use in the invention include: (A) aluminum compounds (*e.g.* aluminum hydroxide, aluminum phosphate, aluminum hydroxyphosphate, oxyhydroxide, orthophosphate, sulfate *etc.* (*e.g.* see chapters 8 & 9 of *Vaccine design: the subunit and adjuvant approach*, eds. Powell & Newman, Plenum Press 1995 (ISBN 0-306-44867-X) (hereinafter "*Vaccine design*"), or mixtures of different aluminum compounds, with the compounds taking any suitable form (*e.g.* gel, crystalline, amorphous *etc.*), and with adsorption being preferred; (B) MF59 (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer) (*see* Chapter 10 of *Vaccine design*; *see also* International patent application WO 90/14837); (C) liposomes (*see* Chapters 13 and 14 of *Vaccine design*); (D) ISCOMs (*see* Chapter 23 of *Vaccine design*); (E) SAF, containing 10% Squalene, 0.4% Tween 80, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized

into a submicron emulsion or vortexed to generate a larger particle size emulsion (*see* Chapter 12 of *Vaccine design*); (F) RibiTM adjuvant system (RAS), (Ribi Immunochem) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (DetoxTM); (G) saponin adjuvants, such as QuilA or QS21 (*see* Chapter 22 of *Vaccine design*), also known as StimulonTM; (H) ISCOMs, which may be devoid of additional detergent (International patent application WO 00/07621); (I) complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA); (J) cytokines, such as interleukins (*e.g.* IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, *etc.*), interferons (*e.g.* interferon- γ), macrophage colony stimulating factor, tumor necrosis factor, *etc.* (*see* Chapters 27 & 28 of *Vaccine design*); (K) microparticles (*see* above); (L) monophosphoryl lipid A (MPL) or 3-O-deacylated MPL (3dMPL) (*e.g.* chapter 21 of *Vaccine design*); (M) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions (European patent applications 0835318, 0735898 and 0761231); (N) oligonucleotides comprising CpG motifs (*see* Krieg (2000) *Vaccine*, 19:618 – 622; Krieg (2001) *Curr. Opin. Mol. Ther.*, 2001, 3:15 – 24; WO 96/02555, WO 98/16247, WO 98/18810, WO 98/40100, WO 98/55495, WO 98/37919 and WO 98/52581, *etc.*) *i.e.* containing at least one CG dinucleotide, with 5-methylcytosine optionally being used in place of cytosine; (O) a polyoxyethylene ether or a polyoxyethylene ester (International patent application WO 99/52549); (P) a polyoxyethylene sorbitan ester surfactant in combination with an octoxynol (International patent application WO 01/21207) or a polyoxyethylene alkyl ether or ester surfactant in combination with at least one additional non-ionic surfactant such as an octoxynol (International patent application WO 01/21152); (Q) an immunostimulatory oligonucleotide (*e.g.* a CpG oligonucleotide) and a saponin (International patent application WO 00/62800); (R) an immunostimulant and a particle of metal salt (International patent application WO 00/23105); (S) a saponin and an oil-in-water emulsion (International patent application WO 99/11241); (T) a saponin (*e.g.* QS21) + 3dMPL + IL-12 (optionally + a sterol) (International patent application WO 98/57659); and (U) other substances that act as immunostimulating agents to enhance the effectiveness of the composition (*e.g.* *see* Chapter 7 of *Vaccine design*).

[0080] Aluminium compounds and MF59 are preferred adjuvants for parenteral use.

[0081] The immunogenic compositions of the invention may be administered in a single dose, or as part of an administration regime. The regime may include priming and boosting doses, which may be administered mucosally, parenterally, or various combinations thereof.

[0082] In some instances the vaccines of the invention may comprise several antigens, fragments or variants encoded by essential genes identified according to the invention. Alternatively, the vaccine may further comprise antigens identified by other methods, or specific to other bacteria, e.g., in order to provide multivalent vaccines.

[0083] With respect to libraries according to the invention, a library of polynucleotides or a library of transposon insertion sites is a collection of sequence information, which information is provided in either biochemical form (e.g., as a collection of polynucleotide molecules), or in electronic form (e.g., as a collection of polynucleotide sequences stored in a computer-readable form, as in a computer system and/or as part of a computer program). The sequence information of the polynucleotides can be used in a variety of ways, for instance as a resource for gene discovery, i.e., for identifying and verifying essential and important genes in *P. aeruginosa*, or for identifying essential or important homologues in other genera or species. A polynucleotide sequence in a library can be a polynucleotide that represents an mRNA, polypeptide, or other gene product encoded by the polynucleotide, and accordingly such a polynucleotide library could be used to formulate corresponding RNA or amino acid libraries according to the sequences of the library members.

[0084] The nucleotide sequence information of the library can be embodied in any suitable form, e.g., electronic or biochemical forms. For example, a library of sequence information embodied in electronic form comprises an accessible computer data file (or, in biochemical form, a collection of nucleic acid molecules) that contains the representative nucleotide sequences of essential and important genes and/or insertion mutants that are differentially expressed (e.g., attenuated growth mutants). Other combinations and comparisons of cells affected by various diseases or stages of disease will be readily apparent to the ordinarily skilled artisan. Biochemical embodiments of the library include a collection of nucleic acids that have the sequences of the genes or

transposon insertion sites in the library, where the nucleic acids can correspond to the entire gene in the library or to a fragment thereof, as described in greater detail below.

[0085] The polynucleotide libraries of the subject invention generally comprise sequence information of a plurality of polynucleotide sequences, where at least one of the polynucleotides has a sequence of any of the sequences in Tables 1-3. By plurality is meant at least 2, usually at least 3 and can include up to all of the sequences included in these tables. The length and number of polynucleotides in the library will vary with the nature of the library, *e.g.*, if the library is an oligonucleotide array, a cDNA array, a computer database of the sequence information, *etc.*

[0086] Where the library is an electronic library, the nucleic acid sequence information can be present in a variety of media. "Media" refers to a manufacture, other than an isolated nucleic acid molecule, that contains the sequence information of the present invention. Such a manufacture provides the genome sequence or a subset thereof in a form that can be examined by means not directly applicable to the sequence as it exists in a nucleic acid. For example, the nucleotide sequence of the present invention, *e.g.* the nucleic acid sequences of any of the polynucleotides of Tables 1-3, can be recorded on computer readable media, *e.g.* any medium that can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as a floppy disc, a hard disc storage medium, and a magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. One of skill in the art can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising a recording of the present sequence information. "Recorded" refers to a process for storing information on computer readable medium, using any such methods as known in the art. Any convenient data storage structure can be chosen, based on the means used to access the stored information. A variety of data processor programs and formats can be used for storage, *e.g.* word processing text file, database format, *etc.* In addition to the sequence information, electronic versions of the libraries of the invention can be provided in conjunction or connection with other computer-readable information and/or other types

of computer-readable files (*e.g.*, searchable files, executable files, *etc.*, including, but not limited to, for example, search program software, *etc.*).

[0087] By providing the nucleotide sequence in computer readable form, the information can be accessed for a variety of purposes. Computer software to access sequence information is publicly available. For example, the gapped BLAST (Altschul *et al. Nucleic Acids Res.* (1997) 25:3389-3402) and BLAZE (Brutlag *et al. Comp. Chem.* (1993) 17:203) search algorithms on a Sybase system can be used to identify open reading frames (ORFs) within the genome that contain homology to ORFs from other organisms.

[0088] As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based system are suitable for use in the present invention. The data storage means can comprise any manufacture comprising a recording of the present sequence information as described above, or a memory access means that can access such a manufacture.

[0089] "Search means" refers to one or more programs implemented on the computer-based system, to compare a target sequence or target structural motif, or expression levels of a polynucleotide in a sample, with the stored sequence information. Search means can be used to identify fragments or regions of the genome that match a particular target sequence or target motif. A variety of known algorithms are publicly known and commercially available, *e.g.* MacPattern (EMBL), BLASTN and BLASTX (NCBI). A "target sequence" can be any polynucleotide or amino acid sequence of six or more contiguous nucleotides or two or more amino acids, preferably from about 10 to 100 amino acids or from about 30 to 300 nucleotides. A variety of comparing means can be used to accomplish comparison of sequence information from a sample (*e.g.*, to analyze target sequences, target motifs, or relative expression levels) with the data storage means. A skilled artisan can readily recognize that any one of the publicly

available homology search programs can be used as the search means for the computer based systems of the present invention to accomplish comparison of target sequences and motifs. Computer programs to analyze expression levels in a sample and in controls are also known in the art.

[0090] A "target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration that is formed upon the folding of the target motif, or on consensus sequences of regulatory or active sites. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited to, hairpin structures, promoter sequences and other expression elements such as binding sites for transcription factors.

[0091] The present invention encompasses the use of the library of essential and important genes to search for polynucleotide and amino acid sequences in common among the essential and important genes. Such identified sequences can be used to design and develop antibacterial agents and vaccines against *Pseudomonas aeruginosa*.

[0092] A variety of structural formats for the input and output means can be used to input and output the information in the computer-based systems of the present invention. One format for an output means ranks the relative expression levels of different polynucleotides. Such presentation provides a skilled artisan with a ranking of relative expression levels to determine a gene expression profile.

[0093] As discussed above, the "library" as used herein also encompasses biochemical libraries of the polynucleotides of Tables 1-3, e.g., collections of nucleic acids representing the provided polynucleotides. The biochemical libraries can take a variety of forms, e.g., a solution of cDNAs, a pattern of probe nucleic acids stably associated with a surface of a solid support (i.e., an array) and the like. Of particular interest are nucleic acid arrays in which one or more of the sequences of Tables 1-3 is represented on the array. By "array" is meant an article of manufacture that has at least a substrate with at least two distinct nucleic acid targets on one of its surfaces, where the number of distinct nucleic acids can be considerably higher, typically being

at least 10 nt, usually at least 20 nt and often at least 25 nt. A variety of different array formats have been developed and are known to those of skill in the art. The arrays of the subject invention find use in a variety of applications, including gene expression analysis, drug screening, mutation analysis and the like, as disclosed in the above-listed exemplary patent documents.

[0094] In addition to the above nucleic acid libraries, analogous libraries of polypeptides are also provided, where the polypeptides of the library will represent at least a portion of the polypeptides encoded by a gene corresponding to one or more of the sequences in Tables 1-3.

[0095] "Identity" as it is used in the present invention should be distinguished from "homology" or "homologous." In the context of the coding sequences and genes of this invention, "homologous" refers to genes whose expression results in expression products which have a combination of amino acid sequence similarity (or base sequence similarity for transcript products) and functional equivalence, and are therefore homologous genes. In general such genes also have a high level of DNA sequence similarity (i.e., greater than 80% identity when such sequences are identified among members of the same genus, but lower when these similarities are noted across bacterial genera), but are not identical. Relationships across bacterial genera between homologous genes are more easily identified at the polypeptide (i.e., the gene product) rather than the DNA level. The combination of functional equivalence and sequence similarity means that if one gene is useful, e.g., as a target for an antibacterial agent, or for screening for such agents, then the homologous gene is probably also useful, but may not react in the same manner or to the same degree to the activity of a specific antibacterial agent.

[0096] Nevertheless, the identification of one such gene serves to identify a homologous gene through the same relationships as indicated above, and can serve as a starting point to determine whether the homologous gene is also essential, whether it responds to the same antibacterial agents, etc. Typically, such homologous genes are found in other bacterial species, especially, but not restricted to, closely related species. Due to the DNA sequence similarity, homologous genes are often identified by

hybridizing with probes from the initially identified gene under hybridizing conditions that allow stable binding under appropriately stringent conditions. For instance, nucleic acids having sequence similarity are detected by hybridization under low stringency conditions, for example, at 50°C and 10XSSC (0.9 M saline/0.09 M sodium citrate) and remain bound when subjected to washing at 55°C in 1XSSC. Sequence identity can be determined by hybridization under stringent conditions, for example, at 50°C or higher and 0.1XSSC (9 mM saline/0.9 mM sodium citrate). Hybridization methods and conditions are well known in the art, see, *e.g.*, USPN 5,707,829. Nucleic acids that are substantially identical to the provided polynucleotide sequences, *e.g.* allelic variants, genetically altered versions of the gene, *etc.*, bind to the provided polynucleotide sequences under stringent hybridization conditions. By using probes, particularly labeled probes of DNA sequences, one can isolate homologous or related or substantially identical genes. The equivalent function of the product is then verified using appropriate biological and/or biochemical assays.

[0097] Using such hybridization technique for the identification of homologous genes, it will be possible to screen other species of bacteria, particularly other genera of gram negative pathogenic bacteria although gram positive bacteria may also be screened, to determine if any essential or important gene identified herein has a homologue in that particular genus of bacteria. If so, such gene could be cloned and isolated for essentiality in the particular genus, and further tested for sensitivity or susceptibility to the antibacterial agents and inhibitors identified herein. Specific genera of bacteria particularly appropriate for hybridization screening for the presence of homologues of essential and important genes include *Escherichia*, *Hemophilus*, *Vibrio*, *Borrelia*, *Enterococcus*, *Helicobacter*, *Legionella*, *Mycobacterium*, *Mycoplasma*, *Neisseria*, *Staphylococcus*, *Streptococcus*, *etc.*

[0098] "Identity," on the other hand, is gauged from the starting point of complete homology. Thereafter, identity may be described in terms of percentages according to the number of base changes in the DNA sequence taking into account any gaps. For purposes of the present invention, variants of the invention have a sequence identity greater than at least about 65%, preferably at least about 75%, more preferably at least about 85%, and can be greater than at least about 90% or more as determined by the

Smith-Waterman homology search algorithm as implemented in MPSRCH program (Oxford Molecular). A preferred method of calculating percent identity is the Smith-Waterman algorithm, using the following. Global DNA sequence identity must be greater than 65% as determined by the Smith-Waterman homology search algorithm as implemented in MPSRCH program (Oxford Molecular) using an affine gap search with the following search parameters: gap open penalty, 12; and gap extension penalty, 1.

[0099] Amino acid sequence variants are also included in the invention. Preferably, naturally or non-naturally occurring protein variants have amino acid sequences which are at least 85%, 90%, or 95% identical to the amino acid sequences identified herein, or to a shorter portion of these sequences. More preferably, the molecules are 98% or 99% identical. Percent sequence identity is determined using the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is taught in Smith and Waterman, *Adv. Appl. Math.* (1981) 2:482-489.

[0100] Also included in the invention are fragments of the nucleic acid sequences and amino acid sequences identified herein, as well as RNAs and RNA fragments corresponding to the DNA sequences disclosed. Such nucleic acid fragments are at least about 10 nucleotides, more preferably at least about 20 to 25 nucleotides, and more preferably at least about 50 to 100 nucleotides, and can include any fragment or variant of a fragment. Such nucleic acid fragments may be used as probes for identifying similar or substantially identical or identical nucleic acid sequences in other genera, or as tools in constructing nucleic acid vectors for knock out and promoter swap experiments. Such amino acid fragments are at least about four amino acids in length, more preferably at least about 8 to 12 amino acids in length, and more preferably at least about 20 to 30 amino acids in length, and may be used as agonists or antagonists to test binding interactions of the proteins disclosed herein, or alternatively as immunogens to isolate antibodies that recognize and bind to specific epitopes of a target protein.

[0101] Once a gene is identified as being essential or important for *Pseudomonas* growth on rich media or in any specific environment, the invention also encompasses the identification of antibacterial agents that have specific activity against the essential or important genes or their gene products or the biochemical pathways in which they are involved. In this context, the term "biochemical pathway" refers to a connected series of biochemical reactions normally occurring in a cell, or more broadly a cellular event such as cellular division or DNA replication. Typically, the steps in such a biochemical pathway act in a coordinated fashion to produce a specific product or products or to produce some other particular biochemical action. Such a biochemical pathway requires the expression product of a gene if the absence of that expression product either directly or indirectly prevents the completion of one or more steps in that pathway, thereby preventing or significantly reducing the production of one or more normal products or effects of that pathway.

[0102] Thus, an agent specifically inhibits such a biochemical pathway requiring the expression product of a particular gene if the presence of the agent stops or substantially reduces the completion of the series of steps in that pathway. Such an agent, may, but does not necessarily, act directly on the expression product of that particular gene. An "expression product" of a gene means that, in a bacterial cell of interest, the gene is transcribed to form RNA molecules. For those genes that are transcribed into mRNAs, the mRNA is translated to form polypeptides. More generally, in this context, "expressed" means that a gene product is formed at the biological level that would normally have the relevant biological activity (i.e., RNA or polypeptide level).

[0103] Thus, the invention includes a method of screening for an antibacterial agent, comprising determining whether a test compound is active against an essential or important bacterial gene identified by the methods herein. The invention also includes a method of screening for an antibacterial agent, comprising determining whether a test compound is active against a protein encoded by an essential bacterial gene identified herein, or active to inhibit the biochemical pathway that involves said protein. The term "antibacterial agent" refers to both naturally occurring antibiotics produced by microorganisms to suppress the growth of other microorganisms, and agents

synthesized or modified in the laboratory which have either bactericidal or bacteriostatic activity. An "active" agent in this context will inhibit the growth of *P. aeruginosa* and possibly related species. The term "inhibiting the growth" indicates that the rate of increase in the numbers of a population of a particular bacterium is reduced. Thus, the term includes situations in which the bacterial population increases but at a reduced rate, as well as situations where the growth of the population is stopped, as well as situations where the numbers of the bacteria in the population are reduced or the population even eliminated. If an enzyme activity assay is used to screen for inhibitors, one can make modifications in uptake/efflux, solubility, half life, etc. to compounds in order to correlate enzyme inhibition with growth inhibition.

[0104] Assays may include any suitable method and may be expected to vary on the type of essential gene or protein involved. For instance, one embodiment is a method comprising the steps of:

- a) contacting said protein or a biologically active fragment thereof with a test compound; and
 - b) determining whether said test compound binds to said essential gene product or protein or fragment of said protein;
- wherein binding of said test compound to said polypeptide or said fragment is indicative that said test compound is an antibacterial agent. It is quite common in identifying antibacterial agents, to assay for binding of a compound to a particular polypeptide where binding is an indication of a compound which is active to modulate the activity of the polypeptide. Binding may be determined by any means according to the agent tested and techniques known in the art.

[0105] Also, agents that inhibit binding of two proteins or polypeptides may also be identified, for instance using a yeast two-hybrid system. Such a system will entail cloning the genes encoding each protein and expressing each in a reporter cell system such that interaction between the two proteins is monitored by observing the expression of a reporter gene. For instance, cDNAs cloned in a yeast two-hybrid expression system (Chien et al. (1991) Proc. Natl. Acad. Sci. (U.S.A.) 88: 9578; Zervos et al. (1993) Cell 72: 233) can be used to identify other cDNAs encoding proteins that

interact with the protein encoded by the first, thereby produce expression of the GAL4-dependent reporter gene. Thereafter, cells expressing both proteins leading to expression of the reporter gene are used to screen for agents that interact with either protein, or the gene encoding either protein. Such systems are well known in the art and are well within the realm of ordinary skill.

[0106] Another embodiment is a method for evaluating a test agent for inhibition of expression of an essential gene identified according to the methods herein, comprising:

- a) contacting a cell expressing said essential gene with said agent; and
- b) determining the amount or level of expression of said essential gene in said sample.

[0107] The exact determination method will be expected to vary depending on the characteristics of the expression product as would be readily apparent to one of ordinary skill in the art. Such methods can include, for example, antibody binding methods, enzymatic activity determinations, and substrate analog binding assays. Such level of expression could be monitored by monitoring the level of the product of the essential gene in the cell, i.e., by SDS-PAGE, or by colorimetric assays using, for example, a *lacZ* gene or protein fusion and detection on media using X-Gal or spectrophotometric detection.

[0108] When such fusions are employed, fusions may be designed using the chromosomal gene so long as the fusion does not disrupt the function of the essential gene, i.e., as with a gene fusion where *lacZ* is inserted just downstream of the essential gene and is expressed from the same promoter as the essential gene. Alternatively, one could employ an extrachromosomal fusion construct whereby the wild type chromosomal copy of the gene is not disrupted. In this case, one could employ a protein fusion, i.e., where a portion of *lacZ* sufficient to be detected with a colorimetric test is fused in frame with the coding region of the essential gene such that a fusion protein is obtained. Other detectable or measurable proteins commonly used in the art may be used as an alternative to *lacZ*, for instance, *phoA*, Lux/luciferase, etc.

[0109] Another method of the invention for evaluating an potential antibacterial agent, comprises the steps of:

- a) providing a bacterial strain comprising a mutant or normal form of the essential or important gene, wherein said mutant form of the gene confers a growth conditional phenotype;
- b) contacting bacteria of said bacterial strain with a test compound in semi-permissive or permissive growth conditions; and
- c) determining whether the growth of said bacterial strain comprising said mutant form of a gene is reduced in the presence of said test compound to a greater extent than a comparison bacteria comprising a normal form of said gene.

[0110] In this context, a "mutant form" of a gene is a gene which has been altered, either naturally or artificially, changing the base sequence of the gene, which results in a change in the amino acid sequence of an encoded polypeptide. The change in the base sequence may be of several different types, including changes of one or more bases for different bases, small deletions, and small insertions. Mutations may also include transposon insertions that lead to attenuated activity, i.e., by resulting in expression of a truncated protein. By contrast, a normal form of a gene is a form commonly found in a natural population of a bacterial strain. Commonly a single form of a gene will predominate in natural populations. In general, such a gene is suitable as a normal form of a gene, however, other forms which provide similar functional characteristics may also be used as a normal gene. In particular, a normal form of a gene does not confer a growth conditional phenotype on the bacterial strain having that gene, while a mutant form of a gene suitable for use in these methods does provide such a growth conditional phenotype.

[0111] As used in the present disclosure, the term "growth conditional phenotype" indicates that a bacterial strain having such a phenotype exhibits a significantly greater difference in growth rates in response to a change in one or more of the culture parameters than an otherwise similar strain not having a growth conditional phenotype. Typically, a growth conditional phenotype is described with respect to a single growth culture parameter, such as temperature. Thus, a temperature (or heat-sensitive) mutant (i.e., a bacterial strain having a heat-sensitive phenotype) exhibits significantly reduced growth, and preferably no growth, under non-permissive temperature conditions as

compared to growth under permissive conditions. In addition, such mutants preferably also show intermediate growth rates at intermediate, or semi-permissive, temperatures. Similar responses also result from the appropriate growth changes for other types of growth conditional phenotypes. A growth conditional phenotype can also be conferred by cloning an essential or important gene behind a regulatable promoter, for instance, a promoter that is only active, or only leads to transcription, under particular environmental conditions or in response to a specific environmental stimulus. Such growth conditional promoter mutants may be isolated according to the promoter swap strategies described herein.

[0112] "Semi-permissive conditions" are conditions in which the relevant culture parameter for a particular growth conditional phenotype is intermediate between permissive conditions and non-permissive conditions. Consequently, in semi-permissive conditions the bacteria having a growth conditional phenotype will exhibit growth rates intermediate between those shown in permissive conditions and non-permissive conditions. In general, such intermediate growth rate is due to a mutant cellular component which is partially functional under semi-permissive conditions, essentially fully functional under permissive conditions, and is non-functional or has very low function under non-permissive conditions, where the level of function of that component is related to the growth rate of the bacteria.

[0113] The term "method of screening" means that the method is suitable, and is typically used, for testing for a particular property or effect in a large number of compounds. Therefore, the method requires only a small amount of time for each compound tested; typically more than one compound may be tested simultaneously (as in a 96-well microtiter plate, or in a series of replica plates), and preferably significant portions of the procedure can be automated. "Method of screening" also refers to determining a set of different properties or effects of one compound simultaneously.

[0114] Because the essential and important genes identified herein can be readily isolated and the genes cloned into a variety of vectors known in the art, the invention also encompasses vectors comprising the nucleic acid sequences, open reading frames and genes of the invention, as well as host cells containing such vectors. Because the

essential genes identified herein can be readily isolated and the encoded gene products expressed by routine methods, the invention also provides the polypeptides encoded by those genes, as well as genes having at least about 50%, or more preferably about 60%, or more preferably about 70%, or more preferably about 80%, or more preferably about 90%, or most preferably about 95% protein sequence identity.

[0115] Thus, by identifying certain essential and/or important genes, this invention provides a method of screening for an antibacterial agent by contacting a polypeptide encoded by one of the identified essential or important genes, or a biologically active fragment of such a polypeptide, with a test compound, and determining whether the test compound binds to the polypeptide or polypeptide fragment. In addition, to simple binding determinations, the invention provides a method for identifying or evaluating an agent active on one of the identified essential genes. The method involves contacting a sample containing an expression product of one of the identified genes with the known or potential agent, and determining the amount or level of activity of the expression product in the sample.

[0116] In particular, antibodies to essential and important gene products are anticipated to be suitable diagnostic binding and antibacterial agents. Thus, antibodies to the proteins encoded by the essential and important genes identified by the methods described herein are also included in the invention. Such antibodies may be isolated according to well known techniques in the art, i.e., Kohler and Milstein for monoclonal antibodies. Also included are polyclonal antibodies and antibody fragments such as Fv, Fab and Fab₂ fragments, as well as chimeric and humanized antibodies, and human antibodies, i.e., made using a Xeno mouse.

[0117] In a further aspect, this invention provides a method of diagnosing the presence of a bacterial strain having one of the genes identified above, by probing with an oligonucleotide at least 15 nucleotides in length, which specifically hybridizes to a nucleotide sequence which is the same as or complementary to the sequence of one of the bacterial genes identified above. In some cases, it is practical to detect the presence of a particular bacterial strain by direct hybridization of a labeled oligonucleotide to the

particular gene. In other cases, it is preferable to first amplify the gene or a portion of the gene before hybridizing labeled oligonucleotides to those amplified copies.

[0118] In a related aspect, this invention provides a method of diagnosing the presence of a bacterial strain by specifically detecting the presence of the transcriptional or translational product of the gene. Typically, a transcriptional (RNA) product is detected by hybridizing a labeled RNA or DNA probe to the transcript. Detection of a specific translational (protein) product can be performed by a variety of different tests depending on the specific protein product. Examples would be binding of the product by specific labeled antibodies and, in some cases, detection of a specific reaction involving the protein product. Diagnostic assays find particular use in assaying tissue and fluid samples of patients suspect of having a *Pseudomonas* infection.

[0119] Antibacterial agents identified according to the methods of the invention may be employed in pharmaceutical compositions. Such compositions may be administered to patients in order to treat an infection by or involving *P. aeruginosa*, either alone or in combination with secondary agents targeted at, for instance virulence factors of *P. aeruginosa*, or other bacteria that may be present in addition to *P. aeruginosa*. In this context, the term "administration" or "administering" refers to a method of giving a dosage of an antibacterial pharmaceutical composition to a mammal, where the method is, e.g., topical, oral, intranasal, inhaled, intravenous, transdermal, intraperitoneal, or intramuscular. The preferred method of administration can vary depending on various factors, e.g., the components of the pharmaceutical composition, the site of the potential or actual bacterial infection, the bacterium involved, and the severity of an actual bacterial infection.

[0120] As used above and throughout this application, "hybridize" has its usual meaning from molecular biology. It refers to the formation of a base-paired interaction between nucleotide polymers. The presence of base pairing implies that at least an appreciable fraction of the nucleotides in each of two nucleotide sequences are complementary to the other according to the usual base pairing rules. The exact fraction of the nucleotides which must be complementary in order to obtain stable

hybridization will vary with a number of factors, including nucleotide sequence, salt concentration of the solution, temperature, and pH.

[0121] The term, "DNA molecule", should be understood to refer to a linear polymer of deoxyribonucleotides, as well as to the linear polymer, base-paired with its complementary strand, forming double-strand DNA (dsDNA). The term is used as equivalent to "DNA chain" or "a DNA" or "DNA polymer" or "DNA sequence", so this description of the term meaning applies to those terms also. The term does not necessarily imply that the specified "DNA molecule" is a discrete entity with no bonding with other entities. The specified DNA molecule may have H-bonding interactions with other DNA molecules, as well as a variety of interactions with other molecules, including RNA molecules. In addition, the specified DNA molecule may be covalently linked in a longer DNA chain at one, or both ends. Any such DNA molecule can be identified in a variety of ways, including, by its particular nucleotide sequence, by its ability to base pair under stringent conditions with another DNA or RNA molecule having a specified sequence, or by a method of isolation which includes hybridization under stringent conditions with another DNA or RNA molecule having a specified sequence.

[0122] References to a "portion" of a DNA or RNA chain mean a linear chain which has a nucleotide sequence which is the same as a sequential subset of the sequence of the chain to which the portion refers. Such a subset may contain all of the sequence of the primary chain or may contain only a shorter sequence. The subset will contain at least 15 bases in a single strand. However, by "same" is meant "substantially the same"; deletions, additions, or substitutions of specific nucleotides of the sequence, or a combination of these changes, which affect a small percentage of the full sequence will still leave the sequences substantially the same. Preferably this percentage of change will be less than 20%, more preferably less than 10%, and even more preferably less than 3%. "Same" is therefore distinguished from "identical"; for identical sequences there cannot be any difference in nucleotide sequences.

[0123] As used in reference to nucleotide sequences, "complementary" has its usual meaning from molecular biology. Two nucleotide sequences or strands are

complementary if they have sequences that would allow base pairing between the strands according to the usual pairing rules. This does not require that the strands would necessarily base pair at every nucleotide; two sequences can still be complementary with a low level of base mismatch such as that created by deletion, addition, or substitution of one or a few (up to 5 in a linear chain of 25 bases) nucleotides, or a combination of such changes.

[0124] Other embodiments of the invention will be immediately envisaged by those of skill in the art upon reading the methods and examples to follow. Such examples are merely illustrative of the invention, and should not be construed as limiting the scope of the invention in any way.

Methodology

Generation of Transposon Library

[0125] Transposon insertions were generated using an improved transposon system for *P. aeruginosa* that utilizes a mini-Tn5-type transposon on a delivery vector that does not replicate in *Pseudomonas*. The delivery vector contains a modified transposase gene with three amino acid substitutions that have been shown to increase the frequency of Tn5 insertions. Weinreich et al., 1994, Evidence that cis preference of the Tn5 transposase is caused by nonproductive multimerization, Genes Dev. 8(19): 2363-74. The Tn5 transposase was placed under control of a *lac* promoter and the complete transposable element was minimized to 1.7 kilobases in length, including a tetracycline resistance marker and transcription terminator to prevent read-through into the genome. The transposon vector is delivered to *P. aeruginosa* via conjugation from a suitable *E. coli* host (e.g. SM10 λ pir). Following conjugation, transposon mutants are selected by resistance to tetracycline conferred by the transposable element.

[0126] Libraries were created in both *P. aeruginosa* PAK and PA01. The average diversity of the libraries created using this strategy is estimated to be ~40,000 to ~50,000 independent mutants per conjugation. Care is taken to minimize passage of each transposon conjugation before plating for mutant selection in an effort to minimize

the potential for siblings, i.e., by stopping the conjugation after sufficient time for a single round of conjugation events.

High-Throughput Transposon Insertion Mapping (HTTIM)

[0127] Precise transposon insertion sites were determined by an anchored, semi-random PCR method for amplification of the transposase/genome junction region. O'Toole and Kolter, 1998, Initiation of biofilm formation in *Pseudomonas fluorescens* WCS365 proceeds via multiple, convergent signaling pathways: a genetic analysis, Mol. Microbiol. 28(3): 449-61. The technique, HTTIM, uses both Tn5 specific and semi-random primers with conserved primer tails. A small aliquot of transposon mutant liquid culture is used as a template and amplification of a fragment containing an insertion site is achieved in a two-step process. The PCR product is then sequenced and the insertion site is entered into an Oracle database for analysis. To date, more than 10,000 to 14,000 insertions have been mapped, each insertion representing the disruption of a gene or intergenic region that is not essential for survival on rich media.

[0128] With every insertion added to the map, the regions of the genome containing essential genes, and particularly those containing operons containing essential genes (because of potential polar effects of insertions in upstream genes), begin to become apparent because these regions will not be able to accommodate transposon insertions. Table 1 shows a listing of the open reading frames identified as existing between transposon insertions, as well as an indication of whether the gene has homologues that have been identified in other bacteria pursuant to BLAST sequence database analysis. Open reading frames were tentatively assigned names prior to being identified pursuant to HTTIM analysis, as disclosed in the *Pseudomonas* genome project, and reported in Stover et al., Complete genome sequence of *Pseudomonas aeruginosa* PAO1, an opportunistic pathogen, August 21, 2000, Nature 406: 959-964, herein incorporated by reference in its entirety.

[0128] For instance, the predicted ORFs were examined individually for (1) identity with known genes of *P. aeruginosa* with sequences deposited in GenBank, (2)

similarity with well-characterized genes from other bacteria, or (3) presence of known functional motifs (see <http://www.pseudomonas.com> for complete list). In each case the literature was searched to ensure that the proteins encoded by the homologous genes were functionally characterized to avoid the perpetuation of poorly supported functional assignments. In addition, 61 researchers who were members of the *P. aeruginosa* research community or had experience in particular aspects of bacterial physiology were enlisted for the *Pseudomonas* Community Annotation Project (PseudoCAP) to provide expert assistance and confirmatory information in the genome project for the analysis of identified ORFs and assigned functions.

[0129] The genome project was able to assign a functional class to 54.2% of ORFs. As in other bacterial genomes, a large proportion of the genome (45.8% of ORFs) consists of genes for which no function could be determined or proposed (confidence level 4). Of these, nearly a third (769 ORFs) possess homology to genes of unknown function predicted in other bacterial genomes, and the remainder (32% of ORFs) do not have strong homology with any reported sequence. The 372 ORFs from the entire genome analysis that are known *P. aeruginosa* genes with demonstrated functions (confidence level 1) are primarily genes encoding lipopolysaccharide biosynthetic enzymes, virulence factors, such as exoenzymes and the systems that secrete them, and proteins involved in motility and adhesion. ORFs with strong homology to genes in other organisms with demonstrated functions (confidence level 2; 1,059 ORFs) include those required for DNA replication, protein synthesis, cell-wall biosynthesis and intermediary metabolism.

[0130] The ORFs that provided the most new information about *P. aeruginosa* biology via the genome annotation were those that could be assigned a probable function on the basis of similarity to established sequence motifs, but could not be assigned a definite name (confidence level 3; 1,590 ORFs). Most of these genes encode products that are in one of three functional classes: putative enzymes (405 genes), transcriptional regulators (341 genes) or transporters of small molecules (408 genes). In some cases genomic context provided additional information, allowing us to identify loci that appear to encode systems such as metabolic pathways and secretion systems, although the substrates for such systems could not be identified. The system

for assigning name and putative function to each essential or important gene was gleaned from the *Pseudomonas* genome project data already available.

Statistical Analysis of Putative Essential and Important Genes

[0131] The open reading frames listed in Table 1 are also presented in Table 2, wherein the ORFs are listed in order of length of base pairs from longest to shortest. Also listed in Table 2 is the probability of essentiality assigned to each of the open reading frames. Probability correlates with length of the ORF, such that the longer the ORF, the higher the probability of hitting the ORF in a random transposon mutagenesis experiment, and the higher the confidence level that the ORF represents an essential or an important gene given that no transposon insertions therein were isolated. Statistical confidence levels in essentiality or importance can help narrow the focus in the screening of specific genes, thereby shortening the verification process and the subsequent identification of antibacterial agents specific for that gene or gene product. Thus, one of the benefits of the HTTIM approach is that it is a quantitative approach that lends itself well to statistical analysis.

[0132] The High-Throughput Transposon Insertion Mapping (HTTIM) strategy utilizes a transposon, which is a small, mobile DNA element that randomly inserts into the chromosome. Although HTTIM was performed using a Tn5 transposon, any transposon may be employed so long as its insertion into the chromosome is random, i.e., devoid of hot spots. Reznikoff, W.S., 1993, The Tn5 transposon, *Annu. Rev. Microbiol.* 47: 945-63. Although the Tn5 derivative employed here contained a modified transposase gene with three amino acid substitutions that have been shown to increase the frequency of Tn5 insertions (*see supra*), the frequency of insertion is generally quite low. For instance, mutants with even one insertion occur at a rate of only 1 in 10^5 or 10^6 bacteria, and must be specifically selected from a background of cells with no insertions. Because the frequency of a single insertion is so low, the frequency of a double insertion is so low as to be insignificant.

[0133] When the transposon insertion disrupts one of the 5570 genes in the *Pseudomonas* genome, the function of that gene is lost. If the disrupted gene is essential for growth, the transposon insertion mutant dies and cannot be characterized.

If the transposon disrupts a gene that is non-essential, the mutant survives, grows and the transposon insertion site is mapped. By examining the insertion sites of a large number of transposon mutants, all, of the non-essential *P. aeruginosa* genes can be identified, and by implication, all of the essential genes may be identified as well. Characterization of over 13,000 transposon insertions revealed insertions in 3890 genes and resulted in an even distribution of insertions across the entire length of the genome. The remaining 1658 genes, in which a transposon insertion has never been observed, are candidates of essential genes (30%). See Figure 7, showing a graph illustrating ORF coverage by Tn5 achieved in High-Throughput Transposon Insertion Mapping (HTTIM), wherein 30% of the genes in the genome are candidate essential genes where ORF size is not taken into account in predicting essentiality.

[0134] Because insertion of the transposon used here into the chromosome was proposed to be random, it was possible that some of the 1658 genes that did not receive a transposon insertion were simply not hit by random chance. One cannot truly know that a transposon has no hot spots and is entirely random until the data is analyzed, and the data here confirmed that the Tn5 derivative employed underwent random insertion in *P. aeruginosa*. Thus, the chance that a gene will not be hit by the transposon as a matter of random chance increases as the length of the gene decreases, particularly for very small genes (< 600 base pairs). See Figure 8, Probability of Being an Essential Gene Given No Hit. Thus, by deleting smaller ORFs (< 600 base pairs) in which there is a lower confidence in essentiality, the probability of essentiality goes up while the number of predicted essential genes decreases. Further, the curve in the graph depicted in Figure 8 should level off faster. Thus, in predicting the essentiality of genes from the HTTIM candidate set, the closer one can come to a probability of 1.0 as depicted in Figure 8, the higher the confidence level of essentiality that can be assigned to each gene in the candidate subset. For a representation of the number of ORFs of various lengths in *P. aeruginosa*, see the histogram in Figure 9.

[0135] A Bayesian statistical model for truncated counting data was applied to the candidate essential gene set, and permitted a determination that 16 to 17 percent of *P. aeruginosa* genes are essential. Such a model may therefore be utilized to increase the

statistical confidence that a given gene in the candidate subset is essential. An exemplary statistical model is provided in Example 1.

Physical Methods for Target Gene Validation

[0136] While the above methodology and the database of putative essential and important gene candidates established thereby is believed to be superior to existing methods with regard to the quantity of experimentation required to identify essential and important genes in *Pseudomonas aeruginosa* and the degree of confidence conferred, it should be understood that the methodology described herein can be incorporated into combined protocols with technology known in the art. For instance, the methods for verifying essentiality disclose in WO 01/07651, herein incorporated by reference in its entirety, would be useful as a secondary method to be utilized in combination with the methods described in this disclosure. Alternatively or additionally, one of several approaches may be used to determine whether a particular gene is essential (absolutely required for survival on rich medium) or important (the absence of which results in attenuated growth) to *P. aeruginosa*.

Integration Knockouts

[0137] This is the simplest and most rapid strategy. PCR is used to amplify a small (200-500 base pairs) portion of the coding sequence, or open reading frame (ORF) of the gene of interest. This gene fragment must be centrally located within the ORF--it cannot include either termini of the gene's coding region. This fragment is cloned into a plasmid vector that can replicate in *E. coli*, but not in *Pseudomonas*. The vector used should have a drug resistance marker that is suitable for selection in *Pseudomonas*, and an origin for conjugal transfer. This feature allows the plasmid to be transferred by conjugation from a suitable *E. coli* donor strain to a *Pseudomonas* strain when the two are co-cultured under the appropriate conditions.

[0138] Following conjugation the co-cultured mixture is harvested and plated on media which selects against the *E. coli* donor and for *Pseudomonas* which contain the plasmid. Since the plasmid is incapable of extra-chromosomal replication in *Pseudomonas*, colonies that arise are the result of homologous recombination between the *Pseudomonas* chromosome and the cloned gene fragment on the plasmid. This is referred to as single-crossover recombination; a single recombination event takes place between the plasmid and the chromosome. The result is integration of the plasmid into the bacterial chromosome and disruption of the gene from which the fragment was amplified (Fig. 1).

[0139] Variations of this approach are possible. For instance, one could clone out the entire locus and isolate transposon insertion mutants in *E. coli* using known techniques, i.e., by transposition from the *E. coli* genome, selecting plasmid insertions by mobilizing the vector into a recipient cell that does not contain the transposon or the antibiotic resistance marker encoded by the transposon, and screening the plasmid for insertions in the cloned gene. Thereafter, a similar assay could be performed by screening for double crossover events in *P. aeruginosa* that result in recombination of the transposon into the chromosomal locus from a suicide vector.

[0140] Integration of the plasmid or other insertion at the locus can be confirmed by a relatively rapid PCR-based screen of recombinant colonies. The advantage of this strategy, particularly the plasmid single crossover strategy, is that it requires only amplification of a short stretch of DNA followed by a single cloning step before recombination experiments can be performed. The disadvantage is that if the target gene is essential, no recombinants can be obtained. Failure to obtain recombinants as proof of essentiality is pretty thin evidence. However, if a gene is in fact non-essential, this method will demonstrate that quickly.

Integration Knockouts with Extra-chromosomal Complementation

[0141] This variation of the above method provides more convincing data when the target gene is essential. It employs the same type of non-replicating integration plasmid described above, but recombinations are performed in strains already carrying a second copy of the target gene on an extra-chromosomal plasmid. This second copy can then supply the essential function when the chromosomal copy is disrupted. If disruptions can only be obtained when a complementing plasmid is present and not when a control plasmid is present, this is rather strong evidence that the target gene is essential. The advantage of this method is that you obtain colonies even when your gene is essential. The disadvantage is that construction and sequencing of the complementation plasmid takes additional time.

Integration with a Regulatable Promoter (Promoter Swap)

[0142] This approach also involves selecting for chromosomal integration of non-replicating plasmids via homologous recombination. However, the design of the integrating plasmid is different. In this case, the N-terminal coding sequence (300-500 base pairs) of the target gene is PCR amplified and cloned into a vector downstream of a regulatable promoter, i.e., a *lac* promoter, which is inducible in the presence of IPTG, or an arabinose promoter (pABD), inducible in the presence of arabinose. The activity of the promoter can be modulated by the presence of a specific inducer molecule. The plasmid is conjugated into *Pseudomonas* and integration selected for under conditions where the regulatable promoter is active. The resulting chromosomal integration replaces the target gene's natural promoter with the regulatable promoter from the plasmid (Fig. 2). If the target gene is essential, recombinants can only survive when the inducer molecule is present in their growth media to stimulate gene expression. If the gene is non-essential, the recombinant's growth is independent of the addition of the inducer. The advantage of this strategy is that it requires only amplification of a short stretch of DNA followed by a single cloning step before recombination experiments can be performed.

Examples: Essential Genes Identified**Example 1: A Bayesian Statistical Model for Increasing Statistical Confidence of Essentiality**

[0143] When the Tn5 transposon inserts into the *Pseudomonas* DNA, one of three things happen: 1) The insertion disrupts a nonessential gene. The cell survives to be characterized and the location of the insertion is determined. 2) The insertion disrupts an essential gene. The cell does not survive and the insertion site is not determined. 3) The insertion is in an intergenic region (between genes) and no information is gained. Genes with identified insertions are nonessential genes. However, genes without identified insertions could be essential genes or nonessential genes with zero transposon insertion. To determine the number of essential genes, we have developed a multivariate Bayesian model for truncated Poisson data and applied it to the *Pseudomonas* genome data set. A likelihood gain based searching algorithm was developed to obtain maximum likelihood estimates. The property of the algorithm was studied. Different approaches were compared for both multivariate and univariate approaches.

A. Structure of the Data and Preliminary Considerations

[0144] A transposon Tn5 insertion mutagenesis library was constructed in *Pseudomonas aeruginosa* strains PAK and PAO1. Mutants were randomly picked and their genomic insertion site sequence determined through polymerase chain reaction (PCR) and automated DNA sequencing. BLASTN analysis of transposon/genome junction sequences was used to map the location of the insertions relative to the completed strain PAO1 genome sequence. More than 20,000 mutants were analyzed which resulted in 12,219 independent insertions being mapped. In order to identify essential genes, transposon insertion sites were analyzed with respect to the protein-encoding genes in this organism. A data set consists of the ID of genes, their length in DNA base-pairs, and the number of transposon insertions were obtained from

experiments. The data set consists of 5570 genes with 881 different sizes ranging from 72 to 16884 DNA base-pairs. The distribution of the gene sizes are extremely skewed to the right with majority of the genes being smaller than 2000 DNA base-pairs as shown in Figure 10.

[0145] A randomly selected subset of the data is shown in Table 4, where δ is gene size, x is the observed number of transposon insertions. Insertions to essential genes are not observable since the insertion mutants can not survive for characterization when the transposon is inserted into an essential gene. Therefore, a gene with zero observed transposon insertions can either be an essential gene or a nonessential gene with zero transposon insertion. Consequently, the count of transposon insertions x is truncated with the truncation region being a single element $\{0\}$.

Table 4: A sample of the gene data set

Gene id	δ	x
298	1359	3
4047	618	0
1170	735	1
4953	1044	1
5526	213	0
4624	1707	4
5069	426	3

[0146] Since the insertion into the chromosome of *Pseudomonas aeruginosa* is random (Reznikoff WS. 1993), and the probability of receiving an insertion for a given gene is proportional to its size measured in DNA base-pairs, the number of transposon insertions into a gene is distributed as truncated Poisson with parameter $\lambda\delta$, where δ is the size of the gene and λ is an unknown parameter, which is independent of gene size.

B. A Bayessian Model

[0147] Let R be a measurable subset of the probability space Ω such that a random variable X is observable only if $X \in \Omega \setminus R$. In this example, no observations can be obtained from essential genes, whereas only nonzero observations can be obtained from nonessential genes, the set R consists of a single element $\{0\}$.

1.

a. One Gene Size

[0148] Assume all genes in a genome have same size, δ , and let N be the number of nonessential genes in this genome. Then the observations X_1, X_2, \dots, X_N from the N nonessential genes are i.i.d. $\text{Poisson}(\lambda \cdot \delta)$, of which, all observations of value zero are truncated. The product $\lambda \cdot \delta$ indicates that the probability of a gene receiving an insertion is proportional to its size.

[0149] Let $\{X_1^*, X_2^*, \dots, X_n^*\} \subseteq \{X_1, X_2, \dots, X_N\}$ denote the subset of all nonzero observations. Then this subset composes a random sample of size n from a truncated Poisson distribution whose distribution function can be written as

$$f(x, \lambda \cdot \delta) = e^{-\lambda \delta} \frac{(\lambda \cdot \delta)^x}{x!} / (1 - e^{-\lambda \delta}), \quad x = 1, 2, \dots \quad (3.1)$$

[0150] Let $q = 1 - e^{-\lambda\delta}$ denote the probability that an observation from $\text{Poisson}(\lambda\delta)$ is not truncated, and let $p = 1 - q = e^{-\lambda\delta}$. Then, conditional on the parameters n and N , the likelihood function of the joint distribution of $\{X_1^*, X_2^*, \dots, X_n^*\}$ can be written as

$$L(\lambda | n, N) = (\lambda \cdot \delta)^{\sum_{i=1}^n X_i^*} \left(\frac{p}{q} \right)^n \left(\prod_{i=1}^n X_i^*! \right)^{-1}. \quad (3.2)$$

$$[0151] \text{ Let } S = X_1^* + X_2^* + \dots + X_n^* \quad (3.3)$$

denote the sum of all nonzero observations and notice that n follows a binomial distribution $B(N, q)$. The likelihood function of the joint distribution of $\{n, X_1^*, X_2^*, \dots, X_n^*\}$, conditional on the parameter N , can be obtained as

$$\begin{aligned} L(\lambda | N) &= \binom{N}{n} q^n p^{N-n} (\lambda \cdot \delta)^S \left(\frac{p}{q} \right)^n \left(\prod_{i=1}^n X_i^*! \right)^{-1} \\ &\propto \binom{N}{n} \lambda^S e^{-(\lambda\delta)N}. \end{aligned} \quad (3.4)$$

[0152] The Bayesian model consists of the conditional model (2.4) and a prior distribution of the parameter N . Assuming N , the number of nonessential genes, is binomial $B(M, \gamma)$, where M is the total number of genes of size δ , which is known, and γ is the portion of nonessential genes which is unknown and is independent of gene size, we can write the likelihood function of the joint distribution of $\{n, N, X_1^*, X_2^*, \dots, X_n^*\}$ as

$$L(\gamma, \lambda, N) \propto \binom{M}{N} \binom{N}{n} \gamma^N (1-\gamma)^{M-N} \lambda^S e^{-(\lambda\delta)N}. \quad (3.5)$$

[0153] This is the likelihood function of n nonzero observations from M genes of the same size δ , of which N genes are nonessential. It is easy to see that (3.5) is proportional to the likelihood function of the posterior distribution of N given observations n and S .

2.

b. Multiple Gene Sizes

[0154] For a given genome consists of genes of different sizes, let $\vec{\delta} = (\delta_1, \delta_2, \dots, \delta_g)^T$ denote the vector of g different gene sizes, and let $\vec{M} = (M_1, M_2, \dots, M_g)^T$ the vector of known numbers of total genes, $\vec{N} = (N_1, N_2, \dots, N_g)^T$ the unknown numbers of nonessential genes, $\vec{n} = (n_1, n_2, \dots, n_g)^T$ the numbers of nonzero observations from the nonessential genes, and $\vec{S} = (S_1, S_2, \dots, S_g)^T$ the sums of nonzero observations, as defined in (3.3).

[0155] The likelihood function of the joint distribution of $\{\vec{n}, \vec{N}, \vec{S}\}$ can be written as

$$L(\gamma, \lambda, \vec{N}) \propto \gamma^{\|\vec{N}\|} (1-\gamma)^{\|\vec{M}\| - \|\vec{N}\|} \lambda^{\|\vec{S}\|} e^{-\lambda(\vec{\delta}^T \cdot \vec{N})} \prod_{i=1}^g \binom{M_i}{N_i} \binom{N_i}{n_i} \quad (3.6)$$

where $\|\cdot\|$ is the L_1 norm of a vector, and $\vec{\delta}^T \cdot \vec{N} = \sum_{i=1}^g \delta_i \cdot N_i$.

[0156] Let $\mathfrak{L} = \ln(L)$. Then up to an additive constant, the log likelihood function of the joint distribution of $\{\vec{n}, \vec{N}, \vec{S}\}$ can be written as

$$\begin{aligned} \mathfrak{L}(\gamma, \lambda, \vec{N}) = & \|\vec{N}\| \cdot \ln(\gamma) + (\|\vec{M}\| - \|\vec{N}\|) \cdot \ln(1-\gamma) \\ & + \|\vec{S}\| \cdot \ln(\lambda) - \lambda \cdot (\vec{\delta}^T \cdot \vec{N}) \\ & - \sum_{i=1}^g \ln((M_i - N_i)!) - \sum_{i=1}^g \ln((N_i - n_i)!), \end{aligned} \quad (3.7)$$

where $(\gamma, \lambda, \vec{N})$ are the parameters of interests. The vector \vec{N} is defined on $\{n_i \leq N_i \leq M_i : i=1, 2, \dots, g\}$ and $\mathfrak{L}(\gamma, \lambda, \vec{N})$ is proportional to the likelihood function of the posterior distribution of \vec{N} given \vec{n} and \vec{S} .

[0157] When g is large, say, in the order of hundreds as in the situation we are dealing with in this paper, obtaining the maximum likelihood (ML) estimate of $\tilde{N} = (N_1, N_2, \dots, N_g)^T$ from (3.7) in such a high dimensional parameter space is a very difficult task both theoretically and computationally. In the next section, we will present a stepwise, maximum likelihood gain based method to obtain the ML estimation.

C. ML ESTIMATION OF PARAMETERS

[0158] For any $\tilde{N} = (N_1, N_2, \dots, N_g)^T$, it is easy to verify using (3.7) that the ML estimations of the parameters γ and λ are

$$\hat{\gamma} = \|\tilde{N}\| / \|\tilde{M}\| \quad (4.1)$$

and

$$\hat{\lambda} = \|\tilde{S}\| / (\tilde{S}^T \cdot \tilde{N}) \quad (4.2)$$

respectively. Substituting (4.1) and (4.2) for γ and λ in (3.7), we have

$$\begin{aligned} \mathfrak{Z}^*(\tilde{N}) &\propto \|\tilde{N}\| \cdot \ln(\|\tilde{N}\|) + (\|\tilde{M}\| - \|\tilde{N}\|) \cdot \ln(\|\tilde{M}\| - \|\tilde{N}\|) \\ &\quad - \|\tilde{S}\| \cdot \ln(\tilde{S}^T \cdot \tilde{N}) - \sum_{i=1}^g (\ln((M_i - N_i)!) + \ln((N_i - n_i)!)) \end{aligned} \quad (4.3)$$

[0159] For $1 \leq i \leq g$, define

$$\Delta_i \mathfrak{Z}^*(\tilde{N}) = \mathfrak{Z}^*(\tilde{N} + \tilde{1}_i) - \mathfrak{Z}^*(\tilde{N}) \quad (4.4)$$

for any $\tilde{N} \in \{n_i \leq N_i < M_i, n_j \leq N_j \leq M_j : i \neq j\}$. In equation (4.4), $\tilde{1}_i = (0, \dots, 0, 1, 0, \dots, 0)^T$ with 1 at the i^{th} position. For notational purpose, let

$$\eta(k) = k \cdot \ln(k) + (\|\tilde{M}\| - k) \cdot \ln(\|\tilde{M}\| - k) \quad (4.5)$$

for $\|\bar{n}\| \leq k < \|\bar{M}\|$. Then, (3.4) can be written as

$$\begin{aligned} \Delta_j \mathcal{F}^*(\bar{N}) &= \eta(\|\bar{N}\| + 1) - \eta(\|\bar{N}\|) \\ &\quad - \|\bar{S}\| \cdot \ln(1 + \delta_i / \bar{\delta}^T \cdot \bar{N}) + \ln\left(\frac{M_i - N_i}{N_i - n_i + 1}\right). \end{aligned} \quad (4.6)$$

[0160] To obtain ML estimation of \bar{N} , we define an operator, \oplus , between the observed vector \bar{n} and any integer k with $0 \leq k \leq \|\bar{M}\| - \|\bar{n}\|$ as follows:

$$\begin{aligned} \bar{n} \oplus 0 &= \bar{n}, \\ \bar{n} \oplus 1 &= \{\bar{n} + \bar{1}_i : \Delta_j \mathcal{F}^*(\bar{n}) \geq \Delta_j \mathcal{F}^*(\bar{n}) \text{ for all } j \neq i\}, \text{ and} \\ \bar{n} \oplus k &= (\bar{n} \oplus (k-1)) \oplus 1 \text{ for } k \geq 2. \end{aligned} \quad (4.7)$$

We also define a likelihood-gain function G with $G(0)=0$ and

$$G(k) = \mathcal{F}^*(\bar{n} \oplus k) - \mathcal{F}^*(\bar{n} \oplus (k-1)) \quad (4.8)$$

for $1 \leq k \leq \|\bar{M}\| - \|\bar{n}\|$.

[0161] Using this likelihood-gain function, we can search the ML estimation for \bar{N} as follows:

1. Start with the observation \bar{n} as the initial estimate of \bar{N} , and denote it as \bar{N}^0 .

2. For each gene size δ_i with $n_i < M_i$, $i=1, 2, \dots, g$, calculate a likelihood difference $\Delta_j \mathcal{L}(\bar{N}^0) = \mathcal{L}(\bar{N}^0 + \bar{1}_j) - \mathcal{L}(\bar{N}^0)$ by set $N_i^0 = n_i + 1$ and $N_j^0 = n_j$ for all $j \neq i$.
3. Update the initial values \bar{N}^0 by setting $N_i^0 = N_i^0 + 1$ such that $\Delta_j \mathcal{L}(\bar{N}^0) = \max\{\Delta_j \mathcal{L}(\bar{N}^0), j=1, 2, \dots, g\}$. This maximum likelihood difference is the likelihood gain defined in (4.8).
4. Repeat the process until it converges. By convergence we mean that either the estimated number of nonessential genes equals to the number of genes in each size group or when increasing the number of nonessential genes in any size groups will result in a loss of likelihood.

[0162] This algorithm searches the ML estimator in a high dimensional space (881 in our study) along a path such that at each iteration, it moves in a direction (that is, increases the number of nonessential genes in this size group by one) along which the likelihood gain is maximum among all possible directions. Because the searching algorithm prohibits reversal of previous moves at any later iteration, it moves towards the ML estimator along the shortest path with the deepest ascending (maximum likelihood gain) at each step. Table 5 and Figures 11 and 12 show the values of likelihood gains in each iteration. With very few exceptions where the monotonous is violated only at the fourth or fifth decimal places that probably can be attributed to rounding errors, the likelihood gain is a monotonously decreasing function.

Table 5. A Sample of Likelihood Gains at Each Iteration

Iteration	id	δ	M	n	$\hat{N}(i)$	G(i)
1	28	210	13	2	3	2.67559
2	60	306	14	3	4	2.41082

3	44	258	14	5	6	2.34388
4	63	315	15	5	6	2.29243
...
18	32	222	7	1	2	2.05160
19	81	369	11	2	3	2.05166
...
774	122	492	12	8	11	0.00692
775	266	924	16	14	15	0.00544
776	85	381	14	3	11	0.00531

The following three theorems show that the estimates obtained through the above algorithm are indeed the maximum likelihood estimates.

THEOREM 1: if

$$\sum_{i=1}^g \left(n_i - \exp \left(\frac{\delta_i \cdot \|\bar{S}\|}{\bar{\delta}^T \cdot \bar{n}} \right) \right) > 0, \quad (4.9)$$

then $G(1) > 0$.

Proof: If $G(1) \leq 0$, then by (4.5), $\Delta_i \mathcal{S}^*(\bar{n}) \leq 0$ for all $1 \leq i \leq g$, which leads to

$$\eta(\|\bar{n}\|+1) - \eta(\|\bar{n}\|) - \|\bar{S}\| \cdot \ln \left(1 + \delta_i / (\bar{\delta}^T \cdot \bar{n}) \right) + \ln(M_i - n_i) \leq 0$$

$$\begin{aligned}
&\Rightarrow \|\vec{S}\| \cdot \ln\left(1 + \delta_i / (\vec{\delta}^T \cdot \vec{n})\right) - \ln(M_i - n_i) \geq \eta(\|\vec{n}\| + 1) - \eta(\|\vec{n}\|) \\
&\Rightarrow \frac{\left(1 + \delta_i / (\vec{\delta}^T \cdot \vec{n})\right)^{\|\vec{S}\|}}{M_i - n_i} \geq \frac{(\|\vec{n}\| + 1)^{\|\vec{n}\|+1} \cdot (\|\vec{M}\| - \|\vec{n}\| - 1)^{\|\vec{M}\| - \|\vec{n}\| - 1}}{(\|\vec{n}\|)^{\|\vec{n}\|+1} \cdot (\|\vec{M}\| - \|\vec{n}\|)^{\|\vec{M}\| - \|\vec{n}\| - 1}} \\
&\Rightarrow \sum_{i=1}^g \left(1 + \delta_i / (\vec{\delta}^T \cdot \vec{n})\right)^{\|\vec{S}\|} \geq \\
&\quad \|\vec{n}\| \cdot (1 + 1/\|\vec{n}\|)^{\|\vec{n}\|+1} \cdot (1 + 1/(\|\vec{M}\| - \|\vec{n}\|))^{\|\vec{M}\| - \|\vec{n}\| - 1}
\end{aligned}$$

Using the facts that $(1+1/x)^x < e$, $(1+1/x)^{x+1} > e$, and $(1-1/x)^{x-1} > e^{-1}$ for any $x > 0$, we obtain

$$\begin{aligned}
&\sum_{i=1}^g \exp\left(\frac{\delta_i \cdot \|\vec{S}\|}{\vec{\delta}^T \cdot \vec{n}}\right) \geq \|\vec{n}\| \cdot e \cdot e^{-1} = \|\vec{n}\| \\
&\Rightarrow \sum_{i=1}^g \left(n_i - \exp\left(\frac{\delta_i \cdot \|\vec{S}\|}{\vec{\delta}^T \cdot \vec{n}}\right)\right) < 0
\end{aligned}$$

This is contradictory to condition (4.9).

For $g=1$, (4.9) becomes $\ln(n) > (X_1 + X_2 + \dots + X_n)/n$. Hence, when the mean of the observed transposon insertions is less than the log of the number of nonzero observations, the vector \vec{n} can not be the ML estimator of \vec{N} and there must be truncated observations from nonessential genes.

THEOREM 2:

$$\Delta_i \mathfrak{S}^*(\tilde{N}) > \Delta_i \mathfrak{S}^*(\tilde{N} - \bar{1}_j) \quad \text{for all } i \neq j \quad (4.10)$$

Proof: By definition in (4.5),

$$\frac{d[\eta(x+1) - \eta(x)]}{dx} = \ln \left(\frac{x+1}{x} \cdot \frac{\|\tilde{M}\| - x}{\|\tilde{M}\| - x - 1} \right) > 0$$

for any $0 < x < \|\tilde{M}\|$. Hence $\eta(\|\tilde{N}\| + 1) - \eta(\|\tilde{N}\|)$ is an increase function of $\|\tilde{N}\|$. Using this result, we have

$$\begin{aligned} \Delta_i \mathfrak{S}^*(\tilde{N}) - \Delta_i \mathfrak{S}^*(\tilde{N} - \bar{1}_j) &= \\ &= (\eta(\|\tilde{N}\| + 1) - \eta(\|\tilde{N}\|)) - (\eta(\|\tilde{N}\|) - \eta(\|\tilde{N}\| - 1)) \\ &\quad - \|\tilde{S}\| \cdot \ln(1 + \delta_i / (\tilde{\delta}^T \cdot \tilde{N})) + \|\tilde{S}\| \cdot \ln(1 + \delta_i / (\tilde{\delta}^T \cdot \tilde{N} - \delta_j)) \\ &> \|\tilde{S}\| \cdot [\ln(1 + \delta_i / (\tilde{\delta}^T \cdot \tilde{N} - \delta_j)) - \ln(1 + \delta_i / (\tilde{\delta}^T \cdot \tilde{N}))] > 0 \end{aligned}$$

THEOREM 3: Under (4.9), for any $1 \leq j \leq g$ and $1 \leq k \leq K^*$,

with $K^* = \max\{k^* \geq 0 : G(k) \geq 0 \text{ for all } 0 \leq k \leq k^*\}$,

if $\tilde{N} = \bar{n} \oplus k - \bar{1}_j \in \{n_j \leq N_j \leq M_j\}$, then

$$\mathfrak{S}^*(\bar{n} \oplus k) > \mathfrak{S}^*(\bar{n} \oplus k - \bar{1}_j) \quad (4.11)$$

Proof: This is obviously true when $k=1$. Assume (3.11) is true for integers $1, 2, \dots, k$. For integer $k+1$, we have

$$\begin{aligned} & \mathfrak{I}^*(\bar{n} \oplus (k+1) - \bar{1}_j) - \mathfrak{I}^*(\bar{n} \oplus k) \\ &= [\mathfrak{I}^*(\bar{n} \oplus (k+1) - \bar{1}_j) - \mathfrak{I}^*(\bar{n} \oplus k - \bar{1}_j)] + \\ & \quad [\mathfrak{I}^*(\bar{n} \oplus k - \bar{1}_j) - \mathfrak{I}^*(\bar{n} \oplus k)] \\ &< [\mathfrak{I}^*(\bar{n} \oplus (k+1) - \bar{1}_j) - \mathfrak{I}^*(\bar{n} \oplus k - \bar{1}_j)] \end{aligned}$$

By theorem 2,

$$\mathfrak{I}^*(\bar{n} \oplus (k+1) - \bar{1}_j) - \mathfrak{I}^*(\bar{n} \oplus k - \bar{1}_j) < \mathfrak{I}^*(\bar{n} \oplus (k+1)) - \mathfrak{I}^*(\bar{n} \oplus k)$$

Therefore

$$\mathfrak{I}^*(\bar{n} \oplus (k+1)) > \mathfrak{I}^*(\bar{n} \oplus (k+1) - \bar{1}_j)$$

Combining theorems 1-3, we obtain

THEOREM 4: If the likelihood function defined in (3.7) has an unique solution, the ML estimator of \bar{n} is:

$$\hat{\bar{N}} = \bar{n} \oplus K^* \quad (4.12)$$

[0163] Theorem 3 guarantees that the trajectory of the searching algorithm follows the shortest path in the sense that a reversal of a previous move (that is, removal of a previously added nonessential gene of any gene size) at any later state will result in a loss of likelihood. This property is illustrated in Figure 4 which shows the trajectory of the searching algorithm projected in a subspace spanned by two different gene sizes. For illustration purpose, genes are grouped into 143 groups by grouping genes with similar sizes together to increase the length of the trajectory. As indicated in the plot, at any state, moving backwards in any direction results in a loss of likelihood. Figure 13 shows more trajectories projected in different subspaces.

[0164] Now we need to demonstrate that the likelihood function (3.7), which is defined in a high dimensional discrete space, has an unique solution. This can be established if the same estimations are obtained from different initial values. Since the initial values can be any value between the observation \bar{n} and the total number of genes \bar{M} , we need to extend the searching algorithm (4.7) as follows:

For any initial value $\{\bar{N}^0 : n_i \leq N_i^0 < M_i \text{ for } i=1,2,\dots,g\}$ and any integer k with

$$\begin{aligned} \bar{N}^0 \oplus 0 &= \bar{N}^0, \\ 0 \leq k \leq \|\bar{M}\| - \|\bar{N}^0\| \text{ such that } \bar{N}^0 \oplus 1 &= \{\bar{N}^0 \pm \bar{1}_i : \Delta_r \mathcal{L}^*(\bar{N}^0) \geq \Delta_r \mathcal{L}^*(\bar{N}^0) \text{ for all } j \neq i\}, \text{ and} \\ \bar{N}^0 \oplus k &= (\bar{N}^0 \oplus (k-1)) \oplus 1 \text{ for } k \geq 2. \end{aligned} \quad (4.13)$$

The likelihood gain function is extended similarly as $G(0)=0$ and

$$G(k) = \mathcal{L}^*(\bar{N}^0 \oplus k) - \mathcal{L}^*(\bar{N}^0 \oplus (k-1)) \quad (4.14)$$

for $1 \leq k \leq \|\bar{M}\| - \|\bar{N}^0\|$.

[0165] Algorithm (4.13) preserves all the properties of algorithm (4.7) and it searches the ML estimator the same way as that of algorithm (4.7) with two exceptions. Unlike

algorithm (4.7), which uses \bar{n} as initial values of \bar{N} and at each iteration, the number of nonessential genes is increased by one in gene groups of size δ_i to find the maximum likelihood gain, this algorithm uses \bar{N}^0 as initial values of \bar{N} which can be greater than the ML estimator. Therefore, at each iteration, the number of nonessential genes in a group with size δ_i can be either increased or decreased by one such that the likelihood gain is maximum.

[0166] Randomly selected initial values \bar{N}^0 were used for data with grouped gene sizes and data with exact gene sizes. The estimations of all parameters are exactly the same and the final likelihood for all initial values \bar{N}^0 are exactly the same as indicated in Figure 14, which plots twenty seven different initial values of \bar{N}^0 . The line in the far left represents the likelihood when $\bar{N}^0 = \bar{n}$, and the lines in the middle are randomly selected. Figure 15 is the trajectory projected into a subspace spanned by two gene sizes. Each circle represents the projection of a different initial value \bar{N}^0 . Regardless of the initial values, the trajectories all converge to the ML estimator.

D. ANALYSIS OF PSEUDOMONAS AERUGINOSA DATA

1. Multivariate Model with Exact Gene Sizes

[0167] The data considered here consist of observations from 5570 genes in 881 different sizes, ranging from 72 to 16884 DNA base-pairs. Distribution of gene size is severely skewed to the right as indicated in Figure 10. For many sizes, especially for sizes smaller than 200 or greater than 2000 DNA base-pairs, there is only one gene in a given size and the observation of transposon insertions for small genes are usually truncated. Since all genes are modeled simultaneously in a single model with a prior γ enforcing the essentialness of a gene being independent of its size, the sparseness of the data does not impose limitations on the computation. However, as discussed in the next section, the prior may play a dominating role for small genes where data are sparse.

The estimations of γ and λ , together with the 95 percent BCa confidence intervals are presented in Table 6 and the estimation of \bar{N} is presented in Figure 16.

Table 6. Parameter Estimation of γ and λ

	Estimate	Bias	SE	BCa Confidence Intervals
γ	0.8434	3.942×10^{-3}	9.893×10^{-3}	(0.818, 0.859)
λ	2.547×10^{-3}	-1.027×10^{-5}	4.392×10^{-5}	(0.00247, 0.00264)

Here the bias and standard error are estimated with bootstrap

2. Multivariate Model With Grouped Gene Sizes

[0168] The prior γ plays an important role in enforcing the fact that the essentialness of a gene is independent of its size. It also made possible to estimate the number of essential genes where data are very sparse. However, for small genes where data are extremely sparse, the prior γ becomes the dominating source of information. In order to moderate the dominance of the prior on small genes with sparse observations, we grouped the genes into 143 groups according to their sizes, using the median size of each group as the gene size. Table 7 is a sample of estimated \bar{N} based on grouped and exact gene sizes. In the table, m is the number of unique sizes in each group; N_1 is estimated using grouped data and N_2 is estimated using ungrouped data.

Table 7: Estimated N with Grouped and Exact Gene Sizes

Gene size	m	M	x	N	N_1	N_2
[72, 120]	6	7	3	2	6	7
(120, 150]	4	7	3	2	6	7
(150, 160]	3	7	2	2	6	7
(160, 170]	2	8	0	0	7	7
(170, 180]	3	9	1	1	8	8
(180, 190]	3	9	1	1	8	8
(190, 200]	3	12	4	4	11	11
(200, 210]	4	27	7	7	23	24
(210, 220]	3	19	7	5	16	17
...

[0169] We see that here $N_2 \geq N_1$. However, this is true only for data in the above table where the ungrouped data are extremely sparse and most of the data are truncated. The estimated proportion of non-essential genes, γ , is actually larger for grouped data which is presented in Table 8. Grouping genes with similar sizes reduces the sparseness of the data and consequently, the dominance of the prior. Another obvious advantage of grouping is dimension reduction of the parameter space, and therefore, drastic reduction of computation time. Of course, such grouping introduces another source of variation, and the algorithm could be unrobust against different grouping. In our study, however, different grouping resulted only in slight difference in estimates.

3. Conditional Maximum Likelihood Estimates

For a given gene size δ_j , the likelihood function (3.4) can be written differently as

$$L_j(\gamma, \lambda | N_j) = \binom{N_j}{n_j} q_j^{n_j} p_j^{N_j - n_j} \prod_{i=1}^{n_j} f(x_{j,i}^*, \delta_j \lambda) \quad (5.1)$$

[0170] Here $f(\cdot, \cdot)$ is defined in (3.1), and $x_{j,1}^*, x_{j,2}^*, \dots, x_{j,n_j}^*$ are the n_j nonzero observations from N_j genes of size δ_j . Assume there are g different gene sizes, the likelihood function can be written as

$$L = \left(\prod_{j=1}^g \binom{N_j}{n_j} q_j^{n_j} p_j^{N_j - n_j} \right) \cdot \left(\prod_{j=1}^g \prod_{i=1}^{n_j} f(x_{j,i}^*, \delta_j \lambda) \right) = L_1 \cdot L_2 \quad (5.2)$$

with

$$\sum_{j=1}^g n_j = n.$$

[0171] Assuming the number of observations n_j for each gene size δ_j being fixed, we can obtain the conditional maximum likelihood estimate of λ by maximize L_2 as

$$\hat{\lambda} = \|S\| / \sum_{j=1}^g n_j \frac{\delta_j}{1 - e^{-\lambda \delta_j}}, \quad (5.3)$$

$$\text{where } \|S\| = \sum_{j=1}^g \sum_{i=1}^{n_j} x_{ji}^* = \sum_{i=1}^n x_i^* .$$

Equation (5.3) reduces to equation (4.2) if we estimate N_j by $N_j = \frac{n_j}{1 - e^{-\lambda \delta_j}}$.

The proportion of truncated nonessential genes can be calculated as

$$\hat{p} = P(x=0 | \text{non essential}) = \int_{\Omega} e^{-\lambda \delta} dF(\delta) . \quad (5.4)$$

[0172] Here Ω is the set of nonessential genes, which can be approximated by the set of all untruncated genes.

Therefore,

$$\hat{\gamma} = \frac{n}{M} + \hat{p} \quad (5.5)$$

Estimations from the three approaches are very similar as shown in Table 8. If the primary interest is to estimate λ and γ , the conditional MLE approach has the advantage of simplicity. However, in estimating λ , this approach omitted information of \tilde{M} , and γ is estimated separately after λ is estimated. Another obvious limitation of this approach is that it can only estimate $\|\tilde{N}\|$, the total number of nonessential genes by $\|\tilde{n}\|/\hat{\gamma}$. The estimation of \tilde{N} by $\tilde{n}/\hat{\gamma}$ is not reasonable because even though γ is independent of gene

size, we can not assume the proportion of non-essential genes in different sizes being the same as shown in Figure 17.

Tabl 8. Estimates of γ and λ with the Three Approaches

		Estimates	Bias	SE	95% BCa Confidence intervals
Multivariate Model with					
Exact Gene Sizes	γ	0.843	3.942×10^{-3}	9.893×10^{-3}	(0.818, 0.859)
	λ	2.547×10^{-3}	-1.024×10^{-5}	4.320×10^{-5}	$(2.473, 2.642) \times 10^{-3}$
Multivariate Model with					
Grouped Gene Sizes	γ	0.853	7.221×10^{-4}	8.051×10^{-3}	(0.835, 0.867)
	λ	2.524×10^{-3}	2.803×10^{-6}	4.063×10^{-5}	$(2.451, 2.610) \times 10^{-3}$
Conditional Maximum					
Likelihood Estimates	γ	0.828	-7.621×10^{-5}	7.273×10^{-3}	(0.815, 0.843)
	λ	2.539×10^{-3}	9.713×10^{-7}	4.058×10^{-5}	$(2.455, 2.618) \times 10^{-3}$

E. DISCUSSION OF ONE DIMENSIONAL CASE

[0173] When the model does not depend on gene size, which can happen for example, when we study a subset of genes with a fixed size, or in other settings where the distribution is identical, model (2.6) reduces to (2.5). Blumenthal, Dayhiya, and Gross (1978) studies estimations of complete sample size from an incomplete Poisson sample using conditional, unconditional, and modified maximum likelihood functions. The modified likelihood estimation weights the likelihood function and maximizes it.

This approach is similar to providing priors to λ and N . Table 9 presents four types of estimations of N using data randomly selected from the 143 grouped genes. Here M and n are number of genes and number of genes with at least one observed transposon insertions. N_{m-b} is a subset of N_1 in Table 7, which is estimated using model (2.6) with grouped data; N_b is estimated with model (2.5); N_c and N_u are conditional and unconditional estimates of N as described in Blumenthal., Dayhiya, and Gross (1978).

Table 9: Comparison of Estimations with Different Methods

Gene size	M	n	N_{m-b}	N_b	N_u	N_c
[72, 120]	7	2	6	2	3	2
(400 – 410]	44	31	40	37	36	36
(430 – 440]	46	22	38	25	25	26
(470 – 480]	80	42	66	57	56	57
(500 – 510]	54	30	45	39	39	39
(610 – 620]	47	29	39	33	33	34
(640 – 650]	54	35	45	44	43	43
(710 – 720]	50	35	42	41	41	41
(750 – 760]	56	37	46	39	46	40
(770 – 780]	61	43	51	53	52	52
(910 – 920]	60	47	52	53	53	52
(980 – 990]	57	45	49	52	51	51

(1050 – 1100]	137	107	115	117	115	117
(1200 – 1250]	129	100	106	106	106	106
(1400 – 1450]	121	110	111	112	112	112
(2100 – 2150]	23	20	20	20	20	20

[0174] We see that the estimations from the three univariate models are very similar. For fairly large genes, estimations from the multivariate model are similar to those of the univariate models. However, for small genes with high truncation rate, estimations from the multivariate model are larger than estimations from the univariate models. In the univariate models, only the information related to a particular gene size is used and the estimations are obtained separately for each gene size. This approach tends to underestimate N for small genes with sparse observations. The multivariate model uses a prior to enforce the fact that the essentialness of a gene is independent of its size and maximizes the likelihood jointly for all genes. Therefore, it alleviates the underestimation of N for small genes with high truncation rate.

Example 2: *lpxC*

[0175] Lipid A constitutes the outer layer of the outer membranes of gram-negative bacteria and is essential for bacterial growth. This makes all the enzymes involved in the biosynthesis of this molecule essential for bacterial growth, and therefore ideal targets for drug design. A series of synthetic molecules was previously identified that inhibited the first committed step in lipid A biosynthesis. Onishi H. R., B. A. Pelak, L. S. Gerckens, L. L. Silver, F. M Kahan, M-H Chen, A. A. Patchett, S. M. Galloway, S. A. Hyland, M. S. Anderson, and C. R. H. Raetz. 1996. *Science*. **274**: 980-982. This step is catalyzed by a unique deacetylase (UDP-3-O -[R -3-hydroxymyristoyl]-GlcNAc deacetylase), LpxC.

[0176] UDP-3-O -[R -3-hydroxymyristoyl]-GlcNAc deacetylase (LpxC) is a deacetylase that catalyzes the first committed step of lipopolysaccharide (LPS) biosynthesis in gram negative bacteria. This is the second step following the first

acylation of N-Acetylglucosamine (GlcNAc). This enzyme functions to deacetylate the UDP-3-O -[R -3-hydroxymyristoyl]-GlcNAc. This step was shown to be essential for growth in *E. coli* wherein a point mutant (*EnvA1*) expresses an LpxC protein that has reduced activity. Beall B. and J. Lutkenhaus, 1987. Sequence analysis, transcriptional organization, and insertional mutagenesis of the *envA* gene of *Escherichia coli*. J. Bacteriol. 169: 5408-5415. A 30% reduction in the amount of LPS on the cell wall of such mutants results in hypersensitivity to antibiotics. Attempts to create null mutants in *lpxC* were unsuccessful in a number of pathogenic bacteria, indicating that inhibitors of LpxC would be effective antibiotics for a number of gram negative organisms.

[0177] Previously identified inhibitors are chiral hydroxamic acids that had unique hydrophobic aromatic moieties, and were suspected to bind a metal in the active site of the deacetylase. The most potent inhibitor, L-161,240, displayed a minimal inhibitory concentration of about 1 microgram per milliliter against *E. coli*, caused three logs of bacterial killing in 4 hours, and cured mice infected with a lethal intraperitoneal dose of *E. coli*. Considering the very high degree of homology between the *E. coli* and *P. aeruginosa* enzymes, it was initially presumed that an inhibitor of the *E. coli* enzyme might also inhibit the *P. aeruginosa* enzyme. However, this molecule inhibited LpxC from *P. aeruginosa* only at very high concentrations, and even then it did so poorly. It had no effect on bacterial growth in this organism. Thus, there was some question as to whether the *lpxC* homologue had the same function in *P. aeruginosa*, and whether it was essential to *P. aeruginosa* given its decreased sensitivity to the L,161,240 inhibitor.

[0178] Nevertheless, *P. aeruginosa lpxC* was one nucleic acid identified as being unable to accommodate a transposon insertion in the library depicted in Table 1 (PA4406). To test the essentiality of *P. aeruginosa lpxC*, we first tested the sensitivity of *P. aeruginosa* transformants expressing *E. coli* LpxC following a "promoter swap" integration. Using this technique, we completely shut off expression of the native *P. aeruginosa lpxC*, while expressing only the *E. coli* enzyme encoded on a plasmid. This strategy resulted in a *P. aeruginosa* mutant that was more sensitive to L-161,240. This suggested that the *E. coli lpxC* gene was substituting for the function of the *P. aeruginosa* gene, and moreover, that there were no duplicate functional homologues in *P. aeruginosa* that were active in the absence of *lpxC*.

[0179] Materials. *Pseudomonas aeruginosa* PAO1 was grown at 37°C in Luria-Bertani (LB) broth (Difco) or plated on sheep blood agar (Remel). Tetracycline at 100 µg/ml in LB media was used to maintain the selection of the integrated plasmid pBEM10 in PAO1. LB broth or agar with 10 µg/ml of tetracycline was used for growing *E. coli* DH5α (Gibco BRL) and *E. coli* S-17 transformants. Plasmids pPS72 and pBADHisB were from Promega and Invitrogen, respectively. EDTA, bis-tri buffer, sucrose, arabinose, and DMSO were purchased from Sigma as Ultrapure agents. Yeast extract and Tryptone were obtained from Difco. Restriction enzymes, and T4 DNA Ligase, and their reaction buffers were from New England Biolabs. Polymixin B nonapeptide was from Sigma. The antibiotics, tetracycline, ampicillin, carbenicillin, gentamicin, and kanamycin were all purchased from Sigma. DNA and deduced amino acid information were analyzed using a family of programs included in the Dnastar package. BLASTP was used to search for amino acid similarities among a host of protein databases available on-line through the National Library of Medicine (USA). Altschul, T. F., W. Gish, W. Miller, E. W. Myers, and D. J. Lipman. 1990. Basic local alignment tool. *J. Mol. Biol.* **215**: 403-410.

[0180] DNA manipulations. Standard recombinant DNA procedures were used. Sambrook, J., E. F. Fritsch, and T. Maniatis. 1989. *Molecular cloning: a Laboratory Manual*, 2nd Edition. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory. Primers were designed to the N- and C-terminal regions of the *E. coli* or *P. aeruginosa* *lpxC* gene that encompassed only the coding region and included *Nde*I and *Eco*RI restriction sites for subsequent cloning. For the *E. coli* gene the primers were (5'-GGGAATTCCATATGATCAAACAAGGACACTTAAACGT-3' and 5'-CCGGAATTCTTATGCCAGTACAGCTGAAGGCGCT-3') and for *P. aeruginosa* gene they were (5'-GGGAATTCCATATGATGATCAAACAACGCACCTTGAAGAACAT-3' and 5'-CCGGAATTCCTACACTGCCGCCGCGGGCGCATATAG-3'). These primers were used in a polymerase chain reaction (PCR) containing either *P. aeruginosa* genomic DNA (10-50 µg) or plasmid pKD6 containing the *E. coli* *lpxC* gene (1.0 µg) as template (Sorensen, P. G., J. Lutkenhaus, K. Young, S. S. Eveland, M. S. Anderson,

and C. R. H. Raetz. 1996. Regulation of UDP-3-*O*-[*R*-hydroxymyristoyl]-*N*-acetylglucosamine deacetylase in *Escherichia coli*. The second enzymatic step of lipid A biosynthesis. *J. Biol. Chem.* **271** (42): 25898-25905). The *lpxC* genes were amplified using *Pwo* DNA polymerase (Roche) in a 100 µl reaction mixture containing 200 µM concentration of each dNTP and 0.5 µM concentration of each primer for 30 cycles (94°C denaturation, 55°C annealing, and 72°C polymerization (according to the manufacturer's instructions). The PCR products were purified with the Qiaquick PCR Purification Kit from Qiagen (according to the manufacturer's instructions) and digested with *NdeI* and *EcoRI* restriction enzymes at sites introduced by the primer sequences. Bands of the correct sizes predicted for the *lpxC* genes were separated by gel electrophoresis, and the excised DNA purified using the Qiaquick Gel Extraction Kit from Qiagen (according to the manufacturer's instructions). The purified DNA was ligated into the T7 expression vector (Studier, F. W., A. H. Rosenberg, J.J. Dunn, and J. W. Dubendorff. 1990. Use of T7 RNA polymerase to direct expression of cloned genes. *Methods Enzymol.* **185**: 60-89) pET21b (Novagen), that had been cut in the multiple cloning site with the same enzymes, transformed into DH5α and plated on LB agar containing ampicillin (250 µg/ml). The resulting clones had their DNA sequenced to confirm the fidelity of the PCR reactions before it could be transferred into the expression strain. Subcloning of these fragments into other vectors was carried out as needed for expression in various backgrounds. These included pEX18T (*cbR*) for allelic exchange mutagenesis in *P. aeruginosa* (Schweizer, H. P and T. T. Hoang. 1995. An improved system for gene replacement and *xylE* fusion analysis in *Pseudomonas aeruginosa*. *Gene* **158** (1): 15-22), pDN19 (*tetR*) for low copy number complementation of *E. coli* JBK-1 (Nunn, D., S. Bergman, and S. Lory. 1990. Products of three accessory genes, *pilB*, *pilC*, and *pilD*, are required for biogenesis of *Pseudomonas aeruginosa* pili. *J. Bacteriol.* **172** (6): 2911-2919), and pUCP30T (*gmR*) for *P. aeruginosa* 'promoter swap' mutant complementation (Schweizer, H. P., T. R. Classen, and T. Hoang. 1996. Improved methods for gene analysis and expression in *Pseudomonas*. In: Nakazawa, T., K Furukawa, D. Haas, S. Silver. (Eds.) *Molecular Biology of Pseudomonas*. American Society for Microbiology, Washington, DC. pp. 229-237).

[0181] **Construction of pBEM10 and 'promoter swap' mutagenesis.** Plasmid pPW101 was made by ligating *oriT*, the region that encodes conjugative plasmid transfer, into pSP72 (Promega). *oriT* had been amplified from plasmid pEX100T (Schweizer and Hoang, 1995, *supra*) with an introduction of an *NdeI* and an *AatII* restriction sites. To create the *lpxC* 'promoter swap' vector, pBEM10, the following different DNA pieces were amplified and sequentially ligated into pPW101. These included the tetracycline resistance marker (*tetR*) from plasmid pUCP26 (Olsen, R. H., G. DeBusscher and R. R. McCombie. 1982. Development of broad-host-range vectors and gene banks: self-cloning of the *Pseudomonas aeruginosa* PAO chromosome. J. Bacteriol. **150**: 60-69), the *araBAD* promoter from the plasmid pBAD HisB (Invitrogen) with an altered ribosome binding site (rbs) (Guzman, L.M., D. Belin, M. J. Carson, and J. Beckwith. 1995. Tight regulation, modulation, and high-level expression by vectors containing the arabinose pBAD promoter. J Bacteriol. **177** (14):4121-4130), the *araC* gene, also from pBAD HisB (Lee, N. 1980. Molecular aspects of *ara* regulation. In *The Operon*. J. H. Miller and W. S. Reznikoff, eds. Cold Spring Harbor, NY. Cold Spring Harbor Laboratory, pp. 389-410; and Schleif, R. S. 1992. DNA looping. Ann. Rev. Biochem. **61**: 199-223), and the first 340 base pairs of the *P. aeruginosa lpxC* gene. The *tetR* marker was amplified using a forward primer that introduced a *BglII* site (5'- AGATCTCAAGGGTTGGTTTGCGCA-3') and a reverse primer that introduced an *EcoRI* site (5'- GAATTCTAATTCTCATGTTTGACA-3'). The *araBAD* promoter and *araC* gene were amplified as one piece from the pBAD HisB vector. The forward primer introduced an *XhoI* site (5'-CTCGAGGCATGCATAATGTGCCTGTC-3') and the reverse primer introduced a *HindIII* site (5'- AAGCTTCTCCTGTTAGCCCCAAAAAACG-3'). The rbs was altered from its original AGGAG to CTTCT. The following primer set was used to make these changes and introduced an upstream *BssHII* site (5'- GCGCGCGGACGAAAGTAAACCCAC TGG-3') and a downstream *HindIII* site (5'- AAGCTTATTCAGAAGGTTAGCCCCAAA AAACGGG-3'). The first 340 bases of

PAO1 *lpxC* were amplified from PAO1 genomic DNA. The forward primer introduced a *Hind*III site (5'-AAGCTTATGATCAAACAACGCACCTT-3') and the reverse primer introduced an *Xba*I site (5'-TCTAGAAGCGCTGCCATCCATGATCGG-3'). These pieces were then ligated into pPW101 to form the final product, pBEM10, which was used for the 'promoter swap' mutagenesis of *lpxC*. The 'promoter swap' scheme is a homologous recombination strategy, whereby transformation of pBEM10 into *P. aeruginosa* removed the native *lpxC* promoter and placed the tightly regulated *araBAD* promoter upstream of the chromosomal copy of *lpxC*, allowing modulation of its expression by the use of a simple sugar, arabinose (Figure 3). In the absence of arabinose the *lpxC* was effectively shut off, and expression was inducible by addition of arabinose. Such mutants were selected in the presence of arabinose, and if *lpxC* is essential, these mutants would not be viable in media that is not supplemented with arabinose, but fully capable of growth in the presence of arabinose.

[0182] Growth curves. Bacterial cultures were prepared by diluting stationary phase overnight cultures to an OD₆₀₀ of 0.1 in 5 ml of LB. The inhibitor, L-161,240, was resuspended in DMSO to a final concentration of 10mg/ml and added to the bacterial cultures to a final concentration of 50 µg/ml or 10 µg/ml. In the samples without inhibitor, DMSO was added to keep the final concentration of DMSO equivalent between samples. The cultures were incubated with shaking and 0.8 ml was taken for OD₆₀₀ readings over the course of the experiment. DH5α, PA01, and PA0200 (Schweizer, H. P. 1998. Intrinsic resistance to inhibitors of fatty acid biosynthesis in *Pseudomonas aeruginosa* is due to efflux: application of a novel technique for generation of unmarked chromosomal mutations for the study of efflux systems. Antimicrob. Agents Chemother. 42: 394-398) were all grown at 37°C. In the cases where temperature sensitive JBK strains were being assayed, the cultures were grown at 42°C for both the overnight and the time course cultures.

[0183] Outer membrane permeabilization. Polymixin B nonapeptide (Sigma) was prepared as a suspension in DMSO at 3 mg/ml final concentration. Erythromycin and Tetracycline were resuspended in DMSO to a final concentration of 250 mg/ml and 125 mg/ml, respectively. L-161,240 was prepared as above in DMSO to a final

concentration of 10mg/ml. These DMSO antibiotic solutions were individually added to LB to the appropriate final concentration and mixed. Polymixin B nonapeptide was then added to the appropriate samples and mixed. DMSO was added to each sample to keep the final concentration of DMSO equivalent between samples. A stationary phase overnight culture of PA01 was added to each sample to bring the final concentration to 0.1 OD₆₀₀. Samples were removed for OD₆₀₀ determinations every 1-2 hours for 6.5 hours and the data from these time points were plotted.

[0184] MIC determinations for 'promoter swapped' mutants. Single colonies of DH5 α , PA01 and each promoter swap strain were picked and grown in LB at 37°C with shaking for approximately 4 hours. Assuming that an OD₆₀₀ reading of 1.0 is equivalent to 10⁹ cells/ml, dilutions were made of all cultures to 5x10⁵ cells/ml. 200 μ l of each diluted culture was added to each well where a two-fold serial dilution of inhibitor had been placed. The 96-well plates were incubated at 37°C overnight and their OD₆₀₀ determined using the Spectramax Plus (Molecular Devices) plate reader.

[0185] To confirm the effect of the arabinose-sensitive promoter in regulating the *lpxC* expression in the swapped mutants, MIC determinations were performed as above, except that arabinose was added to induce expression of the chromosomal locus and override the effects of the plasmid borne *lpxC*. In this case the stationary-phase overnight bacterial culture was diluted to 5x10⁵ cells/ml in LB containing Arabinose to a final concentration of 0.2% (a 20% stock made up in water).

RESULTS AND DISCUSSION:

[0186] Homology between the *E. coli* and the *P. aeruginosa* LpxC enzymes. Using protein analysis software, this study and others have compared the deduced amino acid sequence of LpxC from both *E. coli* and *P. aeruginosa* (Hyland, S.A., S. S. Eveland, and M. S. Anderson. 1997. Cloning, expression, and Purification of UDP-3-*O*-Acyl-GlcNAc Deacetylase from *Pseudomonas aeruginosa*: a metalloamidase of the lipid A biosynthesis pathway. J. Bacteriol. 179 (6): 2029-2037). This comparison revealed

82% similarity and 57% identity shared between the two sequences. This homology was found over the entire length of the protein sequence (data not shown). Significant homology with other known acetyl- or acyltransferases was not found, suggesting that LpxC is unique among acetyltransferases. The two proteins also share a total of five fully conserved Histidine residues that are presumed to be responsible for the zinc metal cofactor coordination. It was therefore expected that an inhibitor that functions by chelating the metal cofactor away would affect both enzymes similarly.

[0187] LpxC is essential for growth in *P. aeruginosa*. Since the hydroxamate inhibitor was effective in preventing growth of *E. coli*, but completely ineffective against *P. aeruginosa*, there was a possibility that LpxC was not essential in *P. aeruginosa*. This could be as a result of the presence of another enzyme that catalyzed a similar function. If that were the case, elimination of the LpxC function should be possible without inhibiting bacterial growth. A thorough analysis of the *P. aeruginosa* genome sequence revealed only one LpxC homologue. An attempt to disrupt the function of this LpxC homologue was made by conjugating wild type PAO1 with a suicide vector (pEX18T) carrying *lpxC* whose *Bam*HI - *Sal*I fragment had been replaced with a gentamicin cassette. However, *P. aeruginosa* null mutants could not be established by this method. In several attempts a few gentamicin resistant trans-conjugants were obtained, but in all these cases allelic replacement of the chromosomal *lpxC* by the defective copy had not occurred. Instead, a gene duplication had occurred, placing the suicide vector and the disrupted copy next to the wild type allele (data not shown). This could be demonstrated by the carbenicillin resistance and sucrose sensitivity acquired by these trans-conjugants, both of which are encoded on the suicide vector. These data indicated a strong negative selection for the sought after disruption of *lpxC* suggesting that *lpxC* is essential for growth. To confirm this, an experiment was carried out whereby the trans-conjugants were transformed with either *lpxC* on a low copy, replicating vector, or vector alone. In 100% of *lpxC* transformants, resolution of the gene duplication as demonstrated by the loss of carbenicillin resistance and sucrose sensitivity was observed, as opposed to no such resolution among those

transformed with vector alone. These results suggested that the wild type genomic allele could be disrupted if a functional copy was present on the transforming plasmid.

[0187] In another attempt at demonstrating essentiality of LpxC in *P. aeruginosa*, the 'promoter swap' strategy as described in materials and methods was carried out.

'Promoter swapped' pseudomonas mutants were fully capable of growth in the presence of arabinose when the arabinose sensitive *lpxC* promoter was turned on, but completely incapable of growth in the absence of this inducer. This further confirmed that in *P. aeruginosa*, just as in *E. coli*, LpxC is essential for growth.

[0188] *E. coli* expressing *LpxC* from *P. aeruginosa* is more resistant to L-161, 240. The *E. coli* strain JBK-1/pKD6 contains the chromosomal *lpxC* gene disrupted with a *kan* element and a wild type copy of *E. coli lpxC* on the temperature-sensitive replicon pKD6. The strain was constructed as described by Sorensen *et al.*, 1996. Since *lpxC* is essential for growth, this strain is not viable at 42°C because the functional copy is on the temperature sensitive replicon. Transforming JBK-1/pKD6 with *lpxC* from either *E. coli* or *P. aeruginosa* on a non-temperature-sensitive replicon (pKD19, *TetR*) and selecting at 42°C, produced transformants that were viable at 42°C, tetracycline resistant, and kanamycin sensitive. This result indicated that *lpxC* from *P. aeruginosa* could be expressed in the *E. coli* background, and was capable of substituting for the missing chromosomal copy. An unexpected result was that whereas the JBK-1 carrying the *lpxC* copy from *E. coli* was still sensitive to killing by a slightly higher concentration of L-161,240, the JBK-1 carrying the *lpxC* copy from *P. aeruginosa* was resistant to up to 50 µg/ml, about 50 times above the MIC of the wild type organisms (data not shown). This suggested that the *P. aeruginosa* enzyme was uniquely resistant to this inhibitor. It also meant that this resistance was the reason for the failure to inhibit growth of *P. aeruginosa*, and not reduced permeability, or efflux or modification of drug by the pseudomonal enzymes. This, in turn, suggests that a program designed to search for inhibitors for the pseudomonal enzyme should be based on screening directly on that enzyme, and not the surrogate enzyme from *E. coli*.

[0189] **L-161, 240 is a substrate for the major drug efflux pump of *P. aeruginosa*.** The completed *P. aeruginosa* genome reveals genes for at least nine homologous, multicomponent, multidrug efflux systems (Stover et al., 2000, Complete genome sequence of *Pseudomonas aeruginosa* PA01, an opportunistic pathogen, Nature 406: 959-64). However the only one that is constitutively expressed to a high degree in the wild type strains is MexAB-OprM (Kohler, T., M. Michea-Hamzehpour, and U. Henze. 1997. Characterization of MexE-MexF-OprN, a positively regulated multidrug efflux system of *Pseudomonas aeruginosa*. Mol. Microbiol. 23: 345-354). Therefore, mutants of this efflux system can be used to evaluate the consequences of diminished efflux pump activity. These mutants would be expected to be highly sensitive to a number of antibiotics. Such a mutant, PAO 200, has been isolated (Schweizer, 1998, *supra*), and whereas it shows a higher level of sensitivity to a number of antibiotics (Westbrock-Wadman, S. D. R. Sherman, M. J. Hickey, S. N. Coulter, Y. Q. Zhu, P. Warrenner, L. Y. Nguyen, R. M. Shawar, K. R. Folger, and C. K. Stover . 1999. Characterization of a *Pseudomonas aeruginosa* Efflux Pump Contributing to Aminoglycoside Impermeability. Antimicrobial Agents and Chemotherapy. 43 (12): 2975-2983), it was not more sensitive to L-161,240 (Figure 4). This suggests that this drug compound is not a substrate for this efflux system in *P. aeruginosa*.

[0190] ***P. aeruginosa* is not less permeable to L-161,240.** Low permeability of the outer membrane is a major contributing factor to the observed high levels of intrinsic drug resistance in *P. aeruginosa* (Nikaido, H. 1998. The role of outer membrane and efflux pumps in the resistance of gram-negative bacteria. Can we improve access? Drug Resistance Updates. 1: 93-98). This low permeability is due to the fact that *P. aeruginosa* lacks the homolog of the relatively efficient, trimeric porins like OmpF. *P. aeruginosa* has, instead, OprF, the OmpA homolog, which produces channels only when it is folded into a rare conformation, and only a small fraction of these channels occurs in the open conformation. As is usually the case with *P. aeruginosa* it was assumed that the reason L-161,240 was ineffective against *P. aeruginosa* was the lack of permeability of the outer membrane to this inhibitor. Polymixin B nonapeptide (PMBN), a derivative of Polymixin B that lacks the fatty acid tail, is capable of binding

to the polyanionic LPS molecules and disrupting the bilayer structure, thus increasing the permeability of the outer membrane. PMBN has been used this way to permeabilize the outer membrane of many gram-negative bacteria (Vaara, M. and T. Vaara. 1983. Sensitization of gram-negative bacteria to antibiotics and complement by a nontoxic oligopeptide. *Nature* **303**: 526-528), including *P. aeruginosa* (Viljanen, P. and M. Vaara, 1984. Susceptibility of gram-negative bacteria to polymyxin B nonapeptide. *Antimicro Agents Chemother.* **25**: 701-705) and effectively sensitize them to lipophilic antibiotics. Unlike the acylated polymyxin B, PMBN is not cidal. In order to determine the effect of outer membrane exclusion of L-161,240, we exposed *P. aeruginosa* to PMBN in combination with L-161,240, and with other lipophilic antibiotics as positive controls. Whereas PMBN lowered the MIC of tetracycline for *P. aeruginosa* more than 16 fold, the sensitivity towards L-161,240 remained unchanged (Figure 5). This, together with the *E. coli* expression data indicated that permeability was not a major factor causing the inability of L-161,240 to inhibit pseudomonal growth.

[0191] *P. aeruginosa* expressing only *E. coli* LpxC is more sensitive to L161-240 than wild type. Using the 'promoter swap' technique as described in the methods, it was possible to replace expression from the wild type chromosomal copy of *P. aeruginosa lpxC*, with expression solely from a plasmid borne copy. For this experiment, 'promoter swapped' *P. aeruginosa* was transformed with either vector containing *P. aeruginosa lpxC* ("PA Swap #1"), or vector containing *E. coli lpxC* ("PA Swap #2"). The transformants were then exposed to various concentrations of L-161,240 for MIC determination. Transformants expressing the *E. coli* enzyme only were much more sensitive to the inhibitor compared to organisms expressing the *P. aeruginosa* enzyme (Figure 6). These transformants were sensitive enough to be comparable with the sensitivity seen in *E. coli*. Since the validity of this observation relied on the un-induced arabinose-sensitive promoter to shut down expression from the chromosomal copy of *lpxC*, it was necessary to demonstrate how effectively this happens. To do that, MIC determinations were performed as above, except that arabinose was added to induce expression of the chromosomal locus. For this experiment stationary-phase overnight bacterial cultures were diluted to 5×10^5 cells/ml in LB containing 0.2% arabinose. In this case all the transformants, regardless of what gene the vector contained, were resistant to killing due to the expression of the

chromosomal copy of *P. aeruginosa* *lpxC*. This confirmed that certain intrinsic properties of the *P. aeruginosa* enzyme are resistant to inhibition by this hydroxamate inhibitor. It also confirmed that neither reduced uptake, efflux, nor modification of the inhibitor play a significant role in this observed resistance. Considering the very high similarity between the two enzymes, this finding was not expected.

[0192] But on further examination and analysis of existing data, it was possible to recognize some inherent differences that might explain this finding. Whereas both these enzymes share five conserved Histidine residues, the *E. coli* enzyme has two more Histidines that have no counterparts in the *P. aeruginosa* enzyme. This is an important difference because these residues are probably involved in the metal cofactor coordination. It was also observed earlier that whereas the *E. coli* enzyme is not sensitive to EDTA, the *P. aeruginosa* enzyme was significantly inhibited by as little as 2 μ M EDTA. Evidence that the *E. coli* enzyme is also a metalloenzyme is that the *envA1* mutation, which has one of the conserved Histidines (His 19) replaced by a Serine, is sensitive to EDTA. It was because of these observations that these investigators suggested that the *E. coli* enzyme has a more stably bound metal than that of the EnvA1 mutant protein, and thus it is less accessible to EDTA than the wild type *P. aeruginosa* enzyme. These observations suggest that the Histidine 'patch' that is involved in the metal coordination is not similar between the two enzymes. It is conceivable therefore that since the inhibitor works by chelating the metal cofactor away from the enzyme, each 'patch' has unique features that result in disparate reactivities towards the inhibitor. It is also important to consider the findings of Wyckoff et al., 1998. Hydrocarbon rulers in UDP-*N*-acetylglucosamine acyltransferases. J. Biol. Chem. **273** (49): 32369-32372. These investigators found that LpxA, the first enzyme of lipid A biosynthesis, is very selective for the length of its acyl donor substrates. Whereas *E. coli* LpxA prefers *R*-3-hydroxymyristoyl-ACP to *R*-3-hydroxydecanoyl-ACP, *P. aeruginosa* LpxA prefers the opposite. The products of the LpxA reaction therefore differ in the carbon chain length of their lipid moieties between the two bacteria. Since the product of the LpxA reaction is the substrate of the LpxC reaction, this observation suggests that the two LpxCs would have substrate binding pockets of different sizes to accommodate the different size substrate. That

would, in turn, suggest that inhibitors that have to occupy that active site would be unique for each enzyme.

Examples 3-7: *ispA*, *ispB*, *uppS*, *aroC*, *aroK*, and *metK*

[0193] Several more candidate genes from the HTTIM gene database were tested for essentiality using a single crossover knock-out strategy. The *Pseudomonas* genes targeted for knocking out were *ispA*, *ispB*, *uppS*, *metK*, *aroC*, and *aroK*. To attempt knock-outs, regions of about 300 bp were cloned into the vector pPW120. These regions were selected so that known active site residues (or highly conserved residues likely to be essential for enzyme function) would be separated after generation of a single-crossover knock-out. The regions were (numbering from the start codon): *ispA*, 283-594; *ispB*, 319-610; *uppS*, 103-402; *metK*, 415-732; *aroC*, 385-684; *aroK*, 175-375.

[0194] The pPW120 vector carries an *E. coli* origin of replication, but not a *Pseudomonas* origin of replication, making it a suicide vector. It also carries an origin of conjugal transfer and antibiotic resistance genes for tetracycline and ampicillin. An *E. coli* donor strain (SM10) carrying the pPW120 knockout constructs was incubated with *Pseudomonas* strain PAO1 to allow conjugal transfer, and recombinants were selected by plating onto media containing tetracycline at 100 µg/mL and chloramphenicol at 10 µg/mL. *Pseudomonas* recombinants will be resistant to this antibiotic mixture while wild-type PAO1 and the *E. coli* donor strain will be sensitive. Aromatic amino acid recombinants (*aroC* and *aroK*) were then tested for auxotrophy by plating onto minimal media with and without phenylalanine, tryptophan, tyrosine, and folic acid at 100 µg/mL while maintaining tetracycline selection. The genes *ispB*, *uppS* and *metK* did not yield recombinants, demonstrating that they are essential genes in all media conditions, while *ispA* yielded slow-growing recombinants (suggesting that this gene may nevertheless be an “important” gene according to the invention).

[0195] For *ispA*, *ispB*, *uppS*, and *metK*, the conjugation procedure was also done in the presence of the complementing plasmid pBAD/HisP. This plasmid has both *E. coli* and *Pseudomonas* origins of replication, an antibiotic resistance gene for carbenicillin, and an arabinose-inducible copy of the full-length wild-type gene. In this way,

recombinants with the chromosomal copies of *ispA*, *ispB*, *uppS*, and *metK* knocked out could be isolated since the vector copy would provide complementation.

[0196] The genes *ispB*, *uppS*, and *metK* are novel with regard to *P. aeruginosa*. The gene *ispB* (PA4569, ranging from 5116864 to 5117832 in the genome), has 67% similarity/52% identity to IspB in *E. coli*, and was assigned to the function class concerned with biosynthesis of cofactors, protein groups and carriers, and energy metabolism, with a confidence level of 2. It is thought to be involved in the pathway of ubiquinone biosynthesis.

[0197] The gene *uppS* (PA3652, ranging from 4091654 to 4090899), coding for undecaprenyl pyrophosphate synthetase, has 69% similarity/57% identity to the *uppS* gene in *E. coli*, and was assigned to the function class involved in biosynthesis of cofactors, protein groups and carriers, cell wall and capsule, with a confidence level of 2. It is separated by one gene (*cdsA*) from *dxr*, which is involved in the synthesis of isopentenyl diphosphate, a precursor of undecaprenol phosphate.

[0198] The gene *metK* (PA0546, ranging from 604896 to 603706) had never been characterized in *P. aeruginosa*, although it is 82% similar/72% identical to MetK in *E. coli*. The gene encodes methionine adenosyltransferase (adomet synthetase) which is involved specifically in methionine metabolism, and was originally assigned to a function class of amino acid biosynthesis and metabolism and central intermediate metabolism with a confidence level of 2.

Example 8: *rrf*

[0199] The essentiality of the *P. aeruginosa rrf* (PA3653, ranging from 4092227 to 4091670) gene was tested using the promoter swap methodology disclosed herein. The N-terminus region (position 1-327) of the gene encoding the ribosome recycling factor (*rrf*) was cloned into the plasmid vector pBEM10. A single crossover was constructed as described above for *lpxC*. Recombinants were unable to grow in the absence of arabinose, confirming the essentiality of this gene. The *rrf* gene encodes ribosome recycling factor, alternatively known as ribosome releasing factor, assigned to the functional class pertaining to translation, post-translational modification and

degradation with a confidence level of 1. Although this gene was previously known in *Pseudomonas aeruginosa*, confirming the essentiality of known genes using the methods disclosed herein will reveal new utilities for such genes as targets for the identification and design of new antibacterial drugs.

PA Number	GenBank ID	Protein Name	Gene Name	Alt Gene Name
PA0001	9945819	chromosomal replication initiator protein DnaA	dnaA	
PA0004	9945822	DNA gyrase subunit B	gyrB	
PA0006	9945824	conserved hypothetical protein		yaeD
PA0008	9945826	glycyl-tRNA synthetase beta chain	glyS	
PA0009	9945827	glycyl-tRNA synthetase alpha chain	glyQ	
PA0011	9945830	probable 2-OH-lauroyltransferase		
PA0015	9945834	hypothetical protein		
PA0022	9945841	conserved hypothetical protein		yrdC
PA0026	9945846	hypothetical protein		
PA0033	9945854	hypothetical protein		
PA0035	9945856	tryptophan synthase alpha chain	trpA	
PA0038	9945859	hypothetical protein		
PA0039	9945860	hypothetical protein		
PA0042	9945864	hypothetical protein		
PA0047	9945869	hypothetical protein		
PA0052	9945875	hypothetical protein		
PA0053	9945876	hypothetical protein		
PA0054	9945877	conserved hypothetical protein		yjiI
PA0055	9945878	hypothetical protein		
PA0058	9945881	hypothetical protein		
PA0059	9945882	osmotically inducible protein OsmC	osmC	
PA0060	9945883	conserved hypothetical protein		
PA0061	9945884	hypothetical protein		
PA0065	9945889	hypothetical protein		
PA0068	9945892	hypothetical protein		
PA0069	9945893	conserved hypothetical protein		
PA0070	9945894	hypothetical protein		
PA0080	9945905	hypothetical protein		
PA0082	9945907	hypothetical protein		
PA0094	9945920	hypothetical protein		
PA0098	9945924	hypothetical protein		
PA0100	9945926	hypothetical protein		
PA0105	9945932	cytochrome c oxidase, subunit II	coxB	coll
PA0109	9945936	hypothetical protein		
PA0111	9945938	hypothetical protein		
PA0113	9945940	probable cytochrome c oxidase assembly factor		
PA0114	9945941	conserved hypothetical protein		
PA0115	9945942	conserved hypothetical protein		elaA
PA0116	9945944	hypothetical protein		
PA0119	9945947	probable dicarboxylate transporter		
PA0120	9945948	probable transcriptional regulator		
PA0124	9945952	hypothetical protein		
PA0125	9945953	hypothetical protein		
PA0128	9945956	conserved hypothetical protein		phnA
PA0131	9945960	hypothetical protein		
PA0133	9945962	probable transcriptional regulator		
PA0135	9945964	hypothetical protein		
PA0139	9945969	alkyl hydroperoxide reductase subunit C	ahpC	
PA0143	9945973	probable nucleoside hydrolase		
PA0145	9945975	hypothetical protein		
PA0149	9945980	probable sigma-70 factor, ECF subfamily		

PA0154	9945985	protocatechuate 3,4-dioxygenase, alpha subunit	pcaG	
PA0159	9945991	probable transcriptional regulator		
PA0161	9945993	hypothetical protein		
PA0167	9945999	probable transcriptional regulator		
PA0170	9946003	hypothetical protein		
PA0171	9946004	hypothetical protein		
PA0182	9946016	probable short-chain dehydrogenase		yjgI
PA0183	9946017	arylsulfatase	atsA	
PA0184	9946018	probable ATP-binding component of ABC trans		atsC
PA0187	9946021	hypothetical protein		
PA0188	9946022	hypothetical protein		
PA0200	9946035	hypothetical protein		
PA0202	9946037	probable amidase		
PA0203	9946038	probable binding protein component of ABC tra		
PA0204	9946039	probable permease of ABC transporter		
PA0205	9946040	probable permease of ABC transporter		
PA0207	9946042	probable transcriptional regulator		
PA0209	9946045	conserved hypothetical protein		mdcB
PA0211	9946047	malonate decarboxylase beta subunit	mdcD	
PA0213	9946049	hypothetical protein		mdcG
PA0216	9946052	probable transporter		madM
PA0233	9946071	probable transcriptional regulator		
PA0236	9946074	probable transcriptional regulator		
PA0238	9946076	hypothetical protein		
PA0243	9946082	probable transcriptional regulator		
PA0244	9946083	hypothetical protein		
PA0245	9946084	3-dehydroquinate dehydratase	aroQ2	aroD2
PA0250	9946090	conserved hypothetical protein		
PA0251	9946091	hypothetical protein		
PA0258	9946098	hypothetical protein		
PA0260	9946101	hypothetical protein		
PA0261	9946102	hypothetical protein		
PA0264	9946105	hypothetical protein		
PA0273	9946115	probable MFS transporter		
PA0279	9946122	probable transcriptional regulator		ydfF
PA0280	9946123	sulfate transport protein CysA	cysA	
PA0284	9946127	hypothetical protein		
PA0309	9946155	hypothetical protein		
PA0311	9946157	hypothetical protein		
PA0320	9946167	conserved hypothetical protein		
PA0330	9946178	ribose 5-phosphate isomerase	rplA	
PA0332	9946180	hypothetical protein		
PA0336	9946184	conserved hypothetical protein		ygdP
PA0339	9946187	hypothetical protein		
PA0341	9946190	prolipoprotein diacylglycerol transferase	lgt	umpA
PA0342	9946191	thymidylate synthase	thyA	
PA0350	9946200	dihydrofolate reductase	folA	tmrA
PA0358	9946208	hypothetical protein		
PA0362	9946213	ferredoxin [4Fe-4S]	fdx1	
PA0363	9946214	phosphopantetheine adenylyltransferase	coaD	kdtB
PA0369	9946220	hypothetical protein		
PA0370	9946222	conserved hypothetical protein		yhhF

PA0373	9946225	signal recognition particle receptor FtsY	ftsY	
PA0376	9946228	sigma factor RpoH	rpoH	
PA0377	9946229	hypothetical protein		
PA0380	9946232	conserved hypothetical protein		
PA0384	9946237	hypothetical protein		
PA0398	9946252	hypothetical protein		
PA0402	9946256	aspartate carbamoyltransferase	pyrB	
PA0403	9946257	transcriptional regulator PyrR	pyrR	
PA0404	9946258	conserved hypothetical protein		yqgF
PA0405	9946259	conserved hypothetical protein		yqgE
PA0407	9946262	glutathione synthetase	gshB	
PA0412	9946267	methyltransferase PilK	pilK	
PA0416	9946271	probable transcriptional regulator		chpD
PA0422	9946278	conserved hypothetical protein		
PA0427	9946283	outer membrane protein OprM precursor	oprM	
PA0433	9946290	hypothetical protein		
PA0442	9946300	hypothetical protein		
PA0443	9946301	probable transporter		
PA0445	9946304	probable transposase		
PA0446	9946305	conserved hypothetical protein		
PA0448	9946307	probable transcriptional regulator		
PA0453	9946312	hypothetical protein		
PA0456	9946316	probable cold-shock protein		
PA0466	9946327	hypothetical protein		
PA0474	9946336	hypothetical protein		
PA0475	9946337	probable transcriptional regulator		
PA0477	9946339	probable transcriptional regulator		
PA0479	9946341	probable transcriptional regulator		
PA0488	9946351	conserved hypothetical protein		yfiM
PA0489	9946352	probable phosphoribosyl transferase		
PA0490	9946353	hypothetical protein		
PA0493	9946356	probable biotin-requiring enzyme		
PA0498	9946362	hypothetical protein		
PA0501	9946365	8-amino-7-oxononanoate synthase	bioF	
PA0502	9946366	probable biotin biosynthesis protein bioH		bioH
PA0503	9946367	probable biotin synthesis protein BioC		bioC
PA0504	9946368	dethiobiotin synthase	bioD	
PA0505	9946369	hypothetical protein		
PA0514	9946379	heme d1 biosynthesis protein NirL	nirL	
PA0527	9946393	transcriptional regulator Dnr	dnr	
PA0531	9946397	probable glutamine amidotransferase		
PA0535	9946402	probable transcriptional regulator		
PA0540	9946407	hypothetical protein		
PA0542	9946409	conserved hypothetical protein		yqjC
PA0543	9946410	hypothetical protein		
PA0544	9946411	hypothetical protein		
PA0546	9946414	methionine adenosyltransferase	metK	
PA0550	9946418	conserved hypothetical protein		ygbM
PA0552	9946420	phosphoglycerate kinase	pgk	
PA0553	9946422	hypothetical protein		
PA0555	9946424	fructose-1,6-bisphosphate aldolase	fda	fbaA, cbbA, cfxB
PA0559	9946428	conserved hypothetical protein		yhiN

PA0563	9946432	conserved hypothetical protein		
PA0565	9946434	conserved hypothetical protein		
PA0567	9946437	conserved hypothetical protein		yqaE
PA0570	9946440	hypothetical protein		
PA0571	9946441	hypothetical protein		
PA0574	9946444	hypothetical protein		
PA0578	9946449	conserved hypothetical protein		
PA0579	9946450	30S ribosomal protein S21	rpsU	
PA0580	9946451	O-sialoglycoprotein endopeptidase	gcp	ygjD
PA0582	9946453	dihydroneopterin aldolase	folB	
PA0585	9946456	hypothetical protein		
PA0589	9946461	conserved hypothetical protein		glpE
PA0591	9946463	conserved hypothetical protein		apaG
PA0593	9946465	pyridoxal phosphate biosynthetic protein PdxA	pdxA	
PA0594	9946466	peptidyl-prolyl cis-trans isomerase SurA	surA	
PA0595	9946467	organic solvent tolerance protein OstA precursor	ostA	imp
PA0607	9946481	ribulose-phosphate 3-epimerase	rpe	dod
PA0610	9946484	transcriptional regulator PrtN	prtN	
PA0611	9946485	transcriptional regulator PrtR	prtR	
PA0613	9946487	hypothetical protein		
PA0614	9946488	hypothetical protein		
PA0617	9946492	probable bacteriophage protein		
PA0626	9946501	hypothetical protein		
PA0627	9946502	conserved hypothetical protein		
PA0630	9946505	hypothetical protein		
PA0632	9946507	hypothetical protein		
PA0635	9946511	hypothetical protein		
PA0639	9946515	conserved hypothetical protein		
PA0642	9946518	hypothetical protein		
PA0643	9946519	hypothetical protein		
PA0644	9946520	hypothetical protein		
PA0646	9946523	hypothetical protein		
PA0647	9946524	hypothetical protein		
PA0648	9946525	hypothetical protein		
PA0652	9946529	transcriptional regulator Vfr	vfr	
PA0653	9946530	conserved hypothetical protein		yhfA
PA0655	9946532	hypothetical protein		
PA0660	9946538	hypothetical protein		
PA0661	9946539	conserved hypothetical protein		
PA0665	9946543	conserved hypothetical protein		yadR
PA0678	9946558	probable type II secretion system protein		hxcU
PA0679	9946559	hypothetical protein		hxcP
PA0680	9946560	probable type II secretion system protein		hxcV
PA0684	9946564	probable type II secretion system protein		hxcZ
PA0686	9946566	probable type II secretion system protein		hxcR
PA0687	9946567	probable type II secretion system protein		hxcS
PA0689	9946570	hypothetical protein		
PA0697	9946579	hypothetical protein		
PA0698	9946580	hypothetical protein		
PA0700	9946582	hypothetical protein		
PA0702	9946585	hypothetical protein		
PA0704	9946587	probable amidase		

PA0705	9946588	probable glycosyl transferase		migA
PA0708	9946591	probable transcriptional regulator		
PA0709	9946592	hypothetical protein		
PA0710	9946593	lactoylglutathione lyase	gloA2	
PA0712	9946595	hypothetical protein		
PA0714	9946598	hypothetical protein		
PA0715	9946599	hypothetical protein		
PA0716	9946600	hypothetical protein		
PA0717	9946601	hypothetical protein of bacteriophage Pf1		
PA0720	9946604	helix destabilizing protein of bacteriophage Pf1		
PA0728	9946613	probable bacteriophage integrase		
PA0729	9946614	hypothetical protein		
PA0730	9946615	probable transferase		
PA0733	9946618	probable pseudouridylylase synthase		rsuA
PA0734	9946619	hypothetical protein		
PA0738	9946624	conserved hypothetical protein		
PA0742	9946628	hypothetical protein		
PA0759	9946647	conserved hypothetical protein		
PA0763	9946651	anti-sigma factor MucA	mucA	
PA0767	9946655	GTP-binding protein LepA	lepA	
PA0768	9946656	signal peptidase I	lepB	lep; SPASE I
PA0771	9946660	GTP-binding protein Era	era	
PA0776	9946665	hypothetical protein		
PA0778	9946667	hypothetical protein		
PA0786	9946676	probable transporter		
PA0787	9946677	hypothetical protein		
PA0790	9946681	hypothetical protein		
PA0802	9946694	hypothetical protein		
PA0805	9946697	hypothetical protein		
PA0808	9946701	hypothetical protein		
PA0815	9946708	probable transcriptional regulator		
PA0818	9946712	hypothetical protein		
PA0820	9946714	hypothetical protein		
PA0822	9946716	hypothetical protein		
PA0825	9946719	hypothetical protein		
PA0826	9946720	hypothetical protein		
PA0829	9946723	probable hydrolase		
PA0837	9946732	peptidyl-prolyl cis-trans isomerase SlyD	slyD	
PA0850	9946747	hypothetical protein		
PA0851	9946748	hypothetical protein		
PA0853	9946750	probable oxidoreductase		
PA0857	9946754	morphogene protein BolA	bolA	
PA0862	9946760	hypothetical protein		
PA0867	9946765	hypothetical protein		
PA0868	9946766	conserved hypothetical protein		yaeJ
PA0869	9946767	D-alanyl-D-alanine-endopeptidase	pbpG	
PA0871	9946770	pterin-4-alpha-carbinolamine dehydratase	phhB	
PA0874	9946773	hypothetical protein		
PA0880	9946779	probable ring-cleaving dioxygenase		
PA0894	9946794	hypothetical protein		
PA0900	9946801	hypothetical protein		
PA0903	9946804	alanyl-tRNA synthetase	alaS	sya

PA0904	9946806	aspartate kinase alpha and beta chain	lysC	ask; akaB
PA0905	9946807	carbon storage regulator	csrA	
PA0906	9946808	probable transcriptional regulator		
PA0908	9946810	hypothetical protein		
PA0909	9946811	hypothetical protein		
PA0913	9946815	probable Mg transporter MgtE	mgtE	
PA0922	9946825	hypothetical protein		
PA0927	9946831	D-lactate dehydrogenase (fermentative)	ldhA	ldhD
PA0932	9946836	cysteine synthase B	cysM	
PA0937	9946842	conserved hypothetical protein		yail
PA0939	9946844	hypothetical protein		
PA0944	9946849	phosphoribosylaminoimidazole synthetase	purN	
PA0945	9946850	phosphoribosylaminoimidazole synthetase	purM	
PA0947	9946853	conserved hypothetical protein		
PA0953	9946859	probable thioredoxin		helX
PA0954	9946860	probable acylphosphatase		
PA0956	9946862	prolyl-tRNA synthetase	proS	
PA0960	9946867	hypothetical protein		
PA0962	9946869	probable dna-binding stress protein		
PA0969	9946876	TolQ protein	tolQ	
PA0970	9946877	TolR protein	tolR	
PA0971	9946878	TolA protein	tolA	
PA0972	9946879	TolB protein	tolB	
PA0973	9946880	outer membrane protein OprL precursor	oprL	pal excC
PA0976	9946884	conserved hypothetical protein		
PA0978	9946886	conserved hypothetical protein		
PA0979	9946887	conserved hypothetical protein		
PA0980	9946888	hypothetical protein		
PA0981	9946889	hypothetical protein		
PA0983	9946891	conserved hypothetical protein		
PA0985	9946893	probable colicin-like toxin		
PA0986	9946894	conserved hypothetical protein		
PA0990	9946899	conserved hypothetical protein		
PA0991	9946900	hypothetical protein		
PA0993	9946902	probable pili assembly chaperone		
PA1000	9946909	hypothetical protein		
PA1006	9946916	conserved hypothetical protein		yrkl
PA1008	9946918	bacterioferritin comigratory protein	bcp	
PA1010	9946920	dihydrodipicolinate synthase	dapA	
PA1012	9946922	conserved hypothetical protein		yycJ
PA1013	9946923	phosphoribosylaminoimidazole-succinocarbox	purC	
PA1021	9946932	probable enoyl-CoA hydratase/isomerase		
PA1026	9946938	hypothetical protein		
PA1035	9946948	hypothetical protein		
PA1038	9946951	hypothetical protein		
PA1039	9946952	conserved hypothetical protein		ychJ
PA1049	9946963	pyridoxine 5'-phosphate oxidase	pdxH	
PA1055	9946969	conserved hypothetical protein		phaC
PA1063	9946978	hypothetical protein		
PA1068	9946983	probable heat shock protein (hsp90 family)		
PA1076	9946992	hypothetical protein		
PA1088	9947004	hypothetical protein		

PA1089	9947005	conserved hypothetical protein		
PA1090	9947006	hypothetical protein		
PA1095	9947012	hypothetical protein		fliS
PA1098	9947015	two-component sensor	fleS	
PA1102	9947019	flagellar motor switch protein FliG	fliG	
PA1105	9947022	flagellar protein FliJ	fliJ	
PA1106	9947023	hypothetical protein		
PA1107	9947025	conserved hypothetical protein		
PA1114	9947032	hypothetical protein		
PA1118	9947037	hypothetical protein		
PA1120	9947039	conserved hypothetical protein		yfiN
PA1122	9947041	probable peptide deformylase		def, pdf, fms
PA1125	9947044	probable cobalamin biosynthetic protein		cobB
PA1129	9947049	probable fosfomycin resistance protein		
PA1134	9947054	hypothetical protein		
PA1135	9947055	conserved hypothetical protein		yedU
PA1138	9947058	probable transcriptional regulator		
PA1145	9947066	probable transcriptional regulator		
PA1149	9947071	hypothetical protein		
PA1151	9947073	pyocin S2 immunity protein	imm2	
PA1154	9947076	conserved hypothetical protein		
PA1155	9947077	ribonucleoside reductase, small chain	nrdB	
PA1156	9947078	ribonucleoside reductase, large chain	nrdA	
PA1157	9947080	probable two-component response regulator		
PA1159	9947082	probable cold-shock protein		
PA1160	9947083	hypothetical protein		
PA1162	9947085	succinyl-diaminopimelate desuccinylase	dapE	
PA1164	9947087	conserved hypothetical protein		
PA1165	9947088	hypothetical protein		
PA1167	9947091	hypothetical protein		
PA1168	9947092	hypothetical protein		
PA1172	9947096	cytochrome c-type protein NapC	napC	
PA1173	9947097	cytochrome c-type protein NapB precursor	napB	
PA1176	9947100	ferredoxin protein NapF	napF	
PA1177	9947101	periplasmic nitrate reductase protein NapE	napE	
PA1183	9947108	C4-dicarboxylate transport protein	dctA	
PA1193	9947119	hypothetical protein		
PA1203	9947130	hypothetical protein		
PA1204	9947131	conserved hypothetical protein		yieF
PA1206	9947133	hypothetical protein		
PA1213	9947141	hypothetical protein		
PA1215	9947143	hypothetical protein		
PA1216	9947144	hypothetical protein		
PA1217	9947145	probable 2-isopropylmalate synthase		
PA1219	9947147	hypothetical protein		
PA1223	9947152	probable transcriptional regulator		
PA1224	9947153	probable NAD(P)H dehydrogenase		
PA1228	9947157	hypothetical protein		
PA1230	9947159	hypothetical protein		
PA1233	9947162	hypothetical protein		
PA1237	9947167	probable multidrug resistance efflux pump		
PA1250	9947181	alkaline proteinase inhibitor AprI	aprI	

PA1261	9947193	probable transcriptional regulator		
PA1269	9947202	probable transcriptional regulator		
PA1280	9947214	hypothetical protein		cobC
PA1285	9947220	probable transcriptional regulator		
PA1295	9947231	conserved hypothetical protein		ycgL
PA1298	9947234	conserved hypothetical protein		yohL
PA1300	9947236	probable sigma-70 factor, ECF subfamily		
PA1306	9947243	probable HIT family protein		
PA1307	9947244	conserved hypothetical protein		yafJ
PA1315	9947252	probable transcriptional regulator		
PA1321	9947259	cytochrome o ubiquinol oxidase protein CyoE	cyoE	
PA1323	9947261	hypothetical protein		
PA1328	9947267	probable transcriptional regulator		
PA1331	9947270	conserved hypothetical protein		yegH
PA1342	9947282	probable binding protein component of ABC tra		
PA1348	9947289	hypothetical protein		
PA1349	9947290	conserved hypothetical protein		
PA1350	9947291	hypothetical protein		
PA1352	9947293	conserved hypothetical protein		
PA1353	9947295	hypothetical protein		
PA1355	9947297	hypothetical protein		
PA1358	9947300	hypothetical protein		
PA1362	9947304	hypothetical protein		
PA1364	9947306	probable transmembrane sensor		
PA1366	9947309	hypothetical protein		
PA1369	9947312	hypothetical protein		
PA1370	9947313	hypothetical protein		
PA1371	9947314	hypothetical protein		
PA1372	9947315	hypothetical protein		
PA1375	9947319	erythronate-4-phosphate dehydrogenase	pdxB	
PA1377	9947321	conserved hypothetical protein		yhhY
PA1378	9947322	hypothetical protein		
PA1379	9947323	probable short-chain dehydrogenase		
PA1394	9947340	hypothetical protein		
PA1397	9947343	probable two-component response regulator		
PA1398	9947344	hypothetical protein		
PA1404	9947351	hypothetical protein		
PA1409	9947356	acetyl polyamine aminohydrolase	aphA	
PA1426	9947375	hypothetical protein		
PA1427	9947376	hypothetical protein		
PA1431	9947380	regulatory protein RsaL	rsaL	
PA1432	9947381	autoinducer synthesis protein LasI	lasI	
PA1442	9947393	conserved hypothetical protein		fliL
PA1447	9947398	flagellar biosynthetic protein FliQ	fliQ	
PA1454	9947406	flagellar synthesis regulator FliN		
PA1456	9947408	two-component response regulator CheY	cheY	
PA1461	9947413	probable chemotaxis protein		motB
PA1462	9947414	probable plasmid partitioning protein		
PA1464	9947417	probable purine-binding chemotaxis protein		cheW
PA1465	9947418	hypothetical protein		
PA1468	9947421	hypothetical protein		
PA1472	9947425	conserved hypothetical protein		

PA1475	9947428	heme exporter protein CcmA	ccmA	#NAME?
PA1476	9947429	heme exporter protein CcmB	ccmB	cyt10; cycW; helB
PA1477	9947431	heme exporter protein CcmC	ccmC	pfcyt1 cycZ helC
PA1478	9947432	hypothetical protein		pfcyt2 ccmD cycX helD
PA1480	9947434	cytochrome C-type biogenesis protein CcmF	ccmF	cycK; ccl1
PA1481	9947435	cytochrome C biogenesis protein CcmG	ccmG	dsbE
PA1482	9947436	cytochrome C-type biogenesis protein CcmH	ccmH	ccl2 cycl
PA1488	9947442	hypothetical protein		
PA1489	9947443	hypothetical protein		
PA1492	9947447	hypothetical protein		
PA1496	9947451	probable potassium channel		
PA1504	9947460	probable transcriptional regulator		
PA1508	9947464	hypothetical protein		
PA1509	9947465	hypothetical protein		
PA1514	9947471	conserved hypothetical protein		ybbT
PA1517	9947474	conserved hypothetical protein		
PA1518	9947475	conserved hypothetical protein		
PA1526	9947484	probable transcriptional regulator		
PA1528	9947486	cell division protein ZipA	zipA	
PA1529	9947487	DNA ligase	lig	dnaL ligA
PA1532	9947490	DNA polymerase subunits gamma and tau	dnaX	
PA1533	9947491	conserved hypothetical protein		
PA1535	9947494	probable acyl-CoA dehydrogenase		
PA1539	9947498	hypothetical protein		
PA1540	9947499	conserved hypothetical protein		
PA1541	9947500	probable drug efflux transporter		
PA1548	9947508	conserved hypothetical protein		fixS
PA1551	9947511	probable ferredoxin		fixG
PA1555	9947515	probable cytochrome c		fixP ccoP
PA1558	9947519	hypothetical protein		
PA1559	9947520	hypothetical protein		
PA1560	9947521	hypothetical protein		
PA1564	9947526	conserved hypothetical protein		
PA1568	9947530	conserved hypothetical protein		
PA1571	9947533	hypothetical protein		
PA1581	9947544	succinate dehydrogenase (C subunit)	sdhC	cybA
PA1582	9947545	succinate dehydrogenase (D subunit)	sdhD	
PA1583	9947546	succinate dehydrogenase (A subunit)	sdhA	
PA1584	9947547	succinate dehydrogenase (B subunit)	sdhB	
PA1587	9947550	lipoamide dehydrogenase-glc	lpdG	lpdA
PA1588	9947552	succinyl-CoA synthetase beta chain	sucC	
PA1589	9947553	succinyl-CoA synthetase alpha chain	sucD	
PA1591	9947555	hypothetical protein		
PA1592	9947556	hypothetical protein		
PA1593	9947557	hypothetical protein		
PA1594	9947558	hypothetical protein		
PA1595	9947559	hypothetical protein		
PA1610	9947576	beta-hydroxydecanoyl-ACP dehydrase	fabA	
PA1618	9947584	conserved hypothetical protein		ybdB
PA1619	9947585	probable transcriptional regulator		
PA1622	9947589	probable hydrolase		
PA1623	9947590	conserved hypothetical protein		

PA1624	9947591	hypothetical protein		
PA1630	9947597	probable transcriptional regulator		
PA1632	9947600	KdpF protein	kdpF	
PA1635	9947603	potassium-transporting ATPase, C chain	kdpC	atkC
PA1638	9947606	conserved hypothetical protein		yneH
PA1641	9947610	hypothetical protein		
PA1645	9947614	hypothetical protein		
PA1657	9947627	conserved hypothetical protein		
PA1664	9947635	hypothetical protein		
PA1666	9947637	hypothetical protein		
PA1673	9947645	hypothetical protein		
PA1674	9947646	GTP cyclohydrolase I precursor	folE2	
PA1675	9947647	conserved hypothetical protein		
PA1676	9947648	hypothetical protein		
PA1687	9947660	spermidine synthase	speE	
PA1690	9947663	translocation protein in type III secretion	pscU	
PA1691	9947664	translocation protein in type III secretion	pscT	
PA1696	9947669	translocation protein in type III secretion	pscO	
PA1698	9947672	outer membrane protein PopN	popN	
PA1701	9947675	conserved hypothetical protein in type III secretion		pcr3
PA1702	9947676	conserved hypothetical protein in type III secretion		pcr4
PA1705	9947679	regulator in type III secretion	pcrG	
PA1710	9947684	exoenzyme S synthesis protein C precursor	exsC	
PA1711	9947685	hypothetical protein		
PA1718	9947693	type III export protein PscE	pscE	
PA1719	9947694	type III export protein PscF	pscF	
PA1720	9947695	type III export protein PscG	pscG	
PA1722	9947697	type III export protein PscI	pscI	
PA1732	9947708	conserved hypothetical protein		
PA1733	9947709	conserved hypothetical protein		
PA1743	9947720	hypothetical protein		
PA1745	9947722	hypothetical protein		
PA1747	9947725	hypothetical protein		
PA1750	9947728	phospho-2-dehydro-3-deoxyheptonate aldolase		
PA1757	9947735	homoserine kinase	thrH	
PA1768	9947747	hypothetical protein		
PA1772	9947752	probable methyltransferase		menG
PA1777	9947757	outer membrane protein OprF precursor	oprF	
PA1780	9947760	assimilatory nitrite reductase small subunit	nirD	nasE
PA1783	9947764	nitrate transporter	nasA	nasT
PA1785	9947766	conserved hypothetical protein		nasT
PA1787	9947768	aconitate hydratase 2	acnB	
PA1790	9947772	hypothetical protein		
PA1792	9947774	conserved hypothetical protein		ybbF
PA1794	9947776	glutaminyI-tRNA synthetase	glnS	
PA1795	9947777	cysteinyI-tRNA synthetase	cysS	
PA1796	9947778	5,10-methylene-tetrahydrofolate dehydrogenase	fold	
PA1803	9947786	Lon protease	lon	capR deg muc lopA
PA1815	9947800	ribonuclease H	rnhA	
PA1816	9947801	DNA polymerase III, epsilon chain	dnaQ	mutD
PA1817	9947802	hypothetical protein		
PA1820	9947805	sodium/proton antiporter NhaB	nhaB	

PA1825	9947811	hypothetical protein		
PA1830	9947816	hypothetical protein		
PA1835	9947821	hypothetical protein		
PA1837	9947823	hypothetical protein		
PA1840	9947827	hypothetical protein		
PA1842	9947829	hypothetical protein		
PA1845	9947832	hypothetical protein		
PA1847	9947835	conserved hypothetical protein		yhgl
PA1852	9947840	hypothetical protein		
PA1855	9947843	hypothetical protein		
PA1859	9947848	probable transcriptional regulator		
PA1862	9947851	molybdenum transport protein ModB	modB	
PA1867	9947857	hypothetical protein		xphA
PA1869	9947859	probable acyl carrier protein		
PA1872	9947862	hypothetical protein		
PA1882	9947873	probable transporter		
PA1883	9947874	probable NADH-ubiquinone/plastoquinone oxid		
PA1884	9947875	probable transcriptional regulator		
PA1885	9947876	conserved hypothetical protein		
PA1892	9947884	hypothetical protein		
PA1894	9947886	hypothetical protein		
PA1895	9947887	hypothetical protein		
PA1896	9947888	hypothetical protein		
PA1897	9947889	hypothetical protein		
PA1899	9947892	probable phenazine biosynthesis protein		phzA2
PA1900	9947893	probable phenazine biosynthesis protein		phzB2
PA1905	9950429	probable pyridoxamine 5'-phosphate oxidase		phzG2
PA1911	9947904	probable transmembrane sensor		
PA1912	9947905	probable sigma-70 factor, ECF subfamily		
PA1914	9947907	conserved hypothetical protein		hvn
PA1917	9947910	hypothetical protein		
PA1924	9947918	hypothetical protein		
PA1925	9947919	hypothetical protein		
PA1928	9947923	ribosomal protein alanine acetyltransferase	rimJ	
PA1929	9947924	hypothetical protein		
PA1936	9947932	hypothetical protein		
PA1937	9947933	conserved hypothetical protein		
PA1938	9947934	conserved hypothetical protein		
PA1939	9947935	hypothetical protein		
PA1951	9947949	hypothetical protein		
PA1952	9947950	hypothetical protein		
PA1955	9947953	hypothetical protein		
PA1956	9947954	hypothetical protein		
PA1962	9947960	conserved hypothetical protein		
PA1963	9947962	hypothetical protein		
PA1965	9947964	hypothetical protein		
PA1967	9947966	hypothetical protein		
PA1968	9947967	hypothetical protein		
PA1974	9947974	hypothetical protein		
PA1978	9947978	probable transcriptional regulator		agmR
PA1980	9947980	probable two-component response regulator		
PA1985	9947986	pyrroloquinoline quinone biosynthesis protein PqqA		

PA1986	9947987	pyrroloquinoline quinone biosynthesis protein B	ppqB	
PA1988	9947989	pyrroloquinoline quinone biosynthesis protein D	ppqD	
PA1994	9947996	hypothetical protein		
PA1995	9947997	hypothetical protein		
PA1996	9947998	peptidyl-prolyl cis-trans isomerase C1	ppiC1	
PA2001	9948003	acetyl-CoA acetyltransferase	atoB	
PA2002	9948004	conserved hypothetical protein		atoE
PA2007	9948010	maleylacetoacetate isomerase	maiA	
PA2010	9948013	probable transcriptional regulator		
PA2013	9948016	probable enoyl-CoA hydratase/isomerase		menB
PA2015	9948019	probable acyl-CoA dehydrogenase		
PA2016	9948020	probable transcriptional regulator		
PA2017	9948021	hypothetical protein		
PA2021	9948025	hypothetical protein		
PA2026	9948031	conserved hypothetical protein		yfeH
PA2029	9948034	hypothetical protein		
PA2031	9948036	hypothetical protein		
PA2034	9948039	hypothetical protein		
PA2037	9948043	hypothetical protein		
PA2042	9948048	probable transporter (membrane subunit)		ygjU
PA2051	9948058	probable transmembrane sensor		
PA2052	9948059	cyanate lyase	cynS	
PA2060	9948068	probable permease of ABC transporter		
PA2062	9948071	probable pyridoxal-phosphate dependent enzyme		
PA2066	9948075	hypothetical protein		
PA2071	9948081	elongation factor G	fusA2	
PA2073	9948083	probable transporter (membrane subunit)		
PA2074	9948084	hypothetical protein		
PA2075	9948086	hypothetical protein		
PA2080	9948091	hypothetical protein		
PA2088	9948100	hypothetical protein		
PA2090	9948102	hypothetical protein		
PA2092	9948104	probable MFS transporter		
PA2095	9948108	hypothetical protein		
PA2097	9948110	probable flavin-binding monooxygenase		
PA2101	9948114	conserved hypothetical protein		
PA2103	9948117	probable molybdopterin biosynthesis protein M		moeB
PA2105	9948119	probable acetyltransferase		
PA2107	9948121	hypothetical protein		
PA2110	9948124	hypothetical protein		
PA2118	9948133	O6-methylguanine-DNA methyltransferase	ada	
PA2119	9948134	alcohol dehydrogenase (Zn-dependent)		adh
PA2120	9948135	hypothetical protein		
PA2123	9948138	probable transcriptional regulator		
PA2126	9948142	conserved hypothetical protein		
PA2131	9948147	hypothetical protein		
PA2136	9948153	hypothetical protein		
PA2142	9948159	probable short-chain dehydrogenase		yhxC
PA2143	9948160	hypothetical protein		
PA2146	9948164	conserved hypothetical protein		yciG
PA2149	9948167	hypothetical protein		
PA2157	9948175	hypothetical protein		

PA2161	9948180	hypothetical protein		
PA2166	9948186	hypothetical protein		
PA2167	9948187	hypothetical protein		
PA2170	9948190	hypothetical protein		
PA2171	9948191	hypothetical protein		
PA2174	9948194	hypothetical protein		
PA2175	9948195	hypothetical protein		
PA2182	9948203	hypothetical protein		
PA2183	9948204	hypothetical protein		
PA2184	9948205	conserved hypothetical protein		yciE
PA2185	9948206	hypothetical protein		
PA2186	9948207	hypothetical protein		
PA2187	9948208	hypothetical protein		
PA2190	9948211	conserved hypothetical protein		
PA2192	9948214	conserved hypothetical protein		
PA2196	9948218	probable transcriptional regulator		
PA2197	9948219	conserved hypothetical protein		ycnB
PA2205	9948228	hypothetical protein		
PA2207	9948230	hypothetical protein		
PA2211	9948234	conserved hypothetical protein		
PA2214	9948238	probable MFS transporter		
PA2219	9948243	membrane protein OpdE	opdE	
PA2220	9948244	probable transcriptional regulator		oprR
PA2221	9948245	conserved hypothetical protein		
PA2222	9948247	hypothetical protein		
PA2223	9948248	hypothetical protein		
PA2224	9948249	hypothetical protein		
PA2225	9948250	hypothetical protein		
PA2226	9948251	hypothetical protein		
PA2227	9948252	probable transcriptional regulator		
PA2228	9948253	hypothetical protein		
PA2229	9948254	conserved hypothetical protein		yiiM
PA2234	9948259	probable exopolysaccharide transporter		
PA2242	9948268	hypothetical protein		
PA2245	9948271	hypothetical protein		
PA2251	9948278	hypothetical protein		
PA2253	9948280	L-asparaginase I	ansA	
PA2257	9948284	pyoverdine biosynthesis protein PvcD	pvcD	
PA2258	9948285	transcriptional regulator PtxR	ptxR	
PA2260	9948288	hypothetical protein		
PA2280	9948309	conserved hypothetical protein		arsH
PA2282	9948312	hypothetical protein		
PA2284	9948314	hypothetical protein		
PA2292	9948323	hypothetical protein		
PA2293	9948324	hypothetical protein		
PA2294	9948325	probable ATP-binding component of ABC trans		
PA2295	9948326	probable permease of ABC transporter		
PA2297	9948328	probable ferredoxin		
PA2298	9948329	probable oxidoreductase		
PA2303	9948335	hypothetical protein		
PA2311	9948344	hypothetical protein		
PA2316	9948349	probable transcriptional regulator		

PA2329	9948364	probable ATP-binding component of ABC trans		
PA2331	9948366	hypothetical protein		
PA2336	9948371	hypothetical protein		
PA2338	9948374	probable binding protein component of ABC m		mtIE
PA2343	9948379	xylulose kinase	mtlY	
PA2347	9948384	hypothetical protein		
PA2349	9948386	conserved hypothetical protein		
PA2351	9948388	probable permease of ABC transporter		
PA2365	9948403	conserved hypothetical protein		
PA2367	9948406	hypothetical protein		
PA2368	9948407	hypothetical protein		
PA2370	9948409	hypothetical protein		
PA2372	9948411	hypothetical protein		
PA2375	9948414	hypothetical protein		
PA2383	9948423	probable transcriptional regulator		
PA2391	9948432	probable outer membrane protein		
PA2405	9948449	hypothetical protein		
PA2406	9948450	hypothetical protein		
PA2411	9948455	probable thioesterase		
PA2412	9948456	conserved hypothetical protein		
PA2418	9948463	hypothetical protein		
PA2422	9948467	hypothetical protein		
PA2427	9948473	hypothetical protein		
PA2428	9948474	hypothetical protein		
PA2429	9948475	hypothetical protein		
PA2434	9948480	hypothetical protein		
PA2436	9948482	hypothetical protein		
PA2441	9948488	hypothetical protein		
PA2442	9948489	glycine cleavage system protein T2	gcvT2	
PA2446	9948494	glycine cleavage system protein H2	gcvH2	
PA2451	9948499	hypothetical protein		
PA2453	9948502	hypothetical protein		
PA2455	9948504	hypothetical protein		
PA2456	9948505	hypothetical protein		
PA2459	9948508	hypothetical protein		
PA2460	9948509	hypothetical protein		
PA2461	9948510	hypothetical protein		
PA2464	9948514	hypothetical protein		
PA2467	9948517	probable transmembrane sensor		
PA2469	9948519	probable transcriptional regulator		
PA2473	9948524	probable glutathione S-transferase		
PA2474	9948525	hypothetical protein		
PA2475	9948526	probable cytochrome P450		
PA2485	9948537	hypothetical protein		
PA2487	9948539	hypothetical protein		
PA2490	9948542	conserved hypothetical protein		ydbB
PA2491	9948543	probable oxidoreductase		
PA2492	9948544	transcriptional regulator MexT	mexT	
PA2496	9948549	hypothetical protein		
PA2500	9948553	probable MFS transporter		cynX
PA2501	9948554	hypothetical protein		
PA2504	9948557	hypothetical protein		

PA2507	9948561	catechol 1,2-dioxygenase	catA	
PA2515	9948569	cis-1,2-dihydroxycyclohexa-3,4-diene carboxyl	laxYL	
PA2517	9948571	toluate 1,2-dioxygenase beta subunit	xyLY	
PA2521	9948576	RND divalent metal cation efflux membrane fu	czcB	
PA2536	9948593	probable phosphatidate cytidyltransferase		ynbB
PA2538	9948595	hypothetical protein		
PA2539	9948596	conserved hypothetical protein		ynbD
PA2544	9948602	hypothetical protein		
PA2549	9948608	conserved hypothetical protein		ygiT
PA2551	9948610	probable transcriptional regulator		
PA2552	9948611	probable acyl-CoA dehydrogenase		acdB
PA2553	9948612	probable acyl-CoA thiolase		
PA2554	9948613	probable short-chain dehydrogenase		
PA2577	9948639	probable transcriptional regulator		
PA2584	9948647	CDP-diacylglycerol--glycerol-3-phosphate 3-ph	pgsA	
PA2591	9948655	probable transcriptional regulator		
PA2602	9948667	hypothetical protein		
PA2605	9948670	conserved hypothetical protein		yheN
PA2606	9948671	conserved hypothetical protein		yheM
PA2607	9948672	conserved hypothetical protein		
PA2608	9948673	conserved hypothetical protein		yccK
PA2612	9948677	seryl-tRNA synthetase	serS	
PA2614	9948680	periplasmic chaperone LolA	lolA	
PA2615	9948681	cell division protein FtsK	ftsK	
PA2617	9948683	leucyl/phenylalanyl-tRNA-protein transferase	aat	
PA2619	9948685	initiation factor	infA	
PA2621	9948687	conserved hypothetical protein		
PA2626	9948693	tRNA methyltransferase	trmU	asuE
PA2629	9948696	adenylosuccinate lyase	purB	
PA2638	9948706	NADH dehydrogenase I chain B	nuoB	
PA2641	9948709	NADH dehydrogenase I chain F	nuoF	
PA2645	9948714	NADH dehydrogenase I chain J	nuoJ	
PA2646	9948715	NADH dehydrogenase I chain K	nuoK	
PA2658	9948728	hypothetical protein		
PA2663	9948734	hypothetical protein		
PA2666	9948737	probable 6-pyruvoyl tetrahydrobiopterin syntha		ptpS
PA2667	9948738	conserved hypothetical protein		
PA2668	9948739	hypothetical protein		
PA2673	9948744	probable type II secretion system protein		hplV
PA2674	9948745	probable type II secretion system protein		hplU
PA2675	9948746	probable type II secretion system protein		hplT
PA2678	9948749	probable permease of ABC-2 transporter		
PA2681	9948753	probable transcriptional regulator		
PA2683	9948755	probable serine/threonine dehydratase, degrad		tdcB
PA2689	9948762	hypothetical protein		
PA2690	9948763	probable transposase		
PA2694	9948767	probable thioredoxin		
PA2697	9948771	hypothetical protein		
PA2703	9948777	hypothetical protein		
PA2706	9948780	hypothetical protein		
PA2715	9948790	probable ferredoxin		
PA2719	9948795	hypothetical protein		

PA2720	9948796	hypothetical protein		
PA2721	9948797	hypothetical protein		
PA2722	9948798	hypothetical protein		
PA2723	9948799	hypothetical protein		
PA2726	9948802	probable radical activating enzyme		
PA2730	9948807	hypothetical protein		
PA2731	9948808	hypothetical protein		
PA2733	9948810	conserved hypothetical protein		
PA2734	9948811	hypothetical protein		
PA2736	9948814	hypothetical protein		
PA2737	9948815	conserved hypothetical protein		
PA2738	9948816	integration host factor, alpha subunit	himA	
PA2739	9948817	phenylalanyl-tRNA synthetase, beta subunit	pheT	
PA2740	9948818	phenylalanyl-tRNA synthetase, alpha-subunit	pheS	
PA2741	9948819	50S ribosomal protein L20	rplT	
PA2742	9948820	50S ribosomal protein L35	rpml	
PA2743	9948821	translation initiation factor IF-3	infC	
PA2744	9948822	threonyl-tRNA synthetase	thrS	
PA2749	9948828	DNA-specific endonuclease I	endA	
PA2753	9948832	hypothetical protein		
PA2756	9948835	hypothetical protein		
PA2759	9948839	hypothetical protein		
PA2762	9948842	hypothetical protein		
PA2763	9948843	hypothetical protein		
PA2767	9948847	probable enoyl-CoA hydratase/isomerase		
PA2768	9948848	hypothetical protein		
PA2769	9948849	hypothetical protein		
PA2774	9948855	hypothetical protein		
PA2775	9948856	hypothetical protein		
PA2780	9948861	hypothetical protein		
PA2781	9948862	hypothetical protein		
PA2782	9948863	hypothetical protein		
PA2784	9948866	hypothetical protein		
PA2785	9948867	conserved hypothetical protein		
PA2786	9948868	hypothetical protein		
PA2792	9948874	hypothetical protein		
PA2794	9948877	hypothetical protein		
PA2797	9948880	hypothetical protein		
PA2799	9948882	hypothetical protein		
PA2800	9948883	conserved hypothetical protein		vacJ
PA2803	9948886	hypothetical protein		
PA2805	9948888	hypothetical protein		
PA2807	9948891	hypothetical protein		
PA2808	9948892	hypothetical protein		
PA2811	9948895	probable permease of ABC-2 transporter		yadH
PA2818	9948902	hypothetical protein		
PA2819	9948903	hypothetical protein		
PA2827	9948912	conserved hypothetical protein		yeaA
PA2829	9948914	hypothetical protein		
PA2831	9948917	conserved hypothetical protein		
PA2832	9948918	thiopurine methyltransferase	tpm	
PA2839	9948925	conserved hypothetical protein		ygiD

PA2843	9948930	probable aldolase		
PA2845	9948932	hypothetical protein		
PA2851	9948938	translation elongation factor P	efp	
PA2852	9948939	hypothetical protein		
PA2853	9948941	outer membrane lipoprotein Oprl precursor	oprl	
PA2854	9948942	conserved hypothetical protein		erfK
PA2859	9948947	transcription elongation factor GreB	greB	
PA2863	9948951	lipase modulator protein	lipH	
PA2868	9948957	hypothetical protein		
PA2874	9948963	hypothetical protein		
PA2876	9948966	orotidine 5'-phosphate decarboxylase	pyrF	
PA2877	9948967	probable transcriptional regulator		
PA2879	9948969	probable transcriptional regulator		hpkR
PA2883	9948973	hypothetical protein		
PA2894	9948985	hypothetical protein		
PA2898	9948990	hypothetical protein		
PA2901	9948993	hypothetical protein		
PA2910	9949003	conserved hypothetical protein		yebN
PA2915	9949008	hypothetical protein		
PA2916	9949010	hypothetical protein		
PA2922	9949016	probable hydrolase		
PA2928	9949023	hypothetical protein		
PA2935	9949030	hypothetical protein		
PA2936	9949031	hypothetical protein		
PA2937	9949033	hypothetical protein		
PA2940	9949036	probable acyl-CoA thiolase		
PA2949	9949046	probable lipase		
PA2951	9949048	electron transfer flavoprotein alpha-subunit	etfA	
PA2952	9949049	electron transfer flavoprotein beta-subunit	etfB	
PA2953	9949050	electron transfer flavoprotein-ubiquinone oxidoreductase		
PA2960	9949058	type 4 fimbrial biogenesis protein PilZ	pilZ	
PA2961	9949059	DNA polymerase III, delta prime subunit	holB	
PA2962	9949060	thymidylate kinase	tmk	
PA2963	9949061	conserved hypothetical protein		yceG
PA2966	9949064	acyl carrier protein	acpP	
PA2967	9949065	3-oxoacyl-[acyl-carrier-protein] reductase	fabG	
PA2968	9949066	malonyl-CoA-[acyl-carrier-protein] transacylase	fabD	
PA2970	9949069	50S ribosomal protein L32	rpmF	
PA2971	9949070	conserved hypothetical protein		yceD
PA2975	9949074	ribosomal large subunit pseudouridine synthase	rluC	yceC
PA2977	9949076	UDP-N-acetylpyruvoylglucosamine reductase	murB	
PA2978	9949077	phosphotyrosine protein phosphatase	ptpA	
PA2979	9949078	3-deoxy-manno-octulosonate cytidyltransferase	kdsB	
PA2980	9949079	conserved hypothetical protein		ycaR
PA2981	9949080	tetraacyldisaccharide 4*-kinase	lpxK	
PA2982	9949081	conserved hypothetical protein		
PA2983	9949082	probable tolQ-type transport protein		
PA2985	9949085	hypothetical protein		
PA2986	9949086	conserved hypothetical protein		
PA2987	9949087	probable ATP-binding component of ABC trans		ycfV
PA2988	9949088	conserved hypothetical protein		
PA2989	9949089	hypothetical protein		

PA2991	9949091	soluble pyridine nucleotide transhydrogenase	sth	
PA2992	9949092	hypothetical protein		
PA2996	9949096	Na ⁺ -translocating NADH:uniquinone oxidoreductase	unqrD	
PA3001	9949102	probable glyceraldehyde-3-phosphate dehydrogenase		
PA3004	9949105	probable nucleoside phosphorylase		
PA3009	9949111	hypothetical protein		
PA3011	9949113	DNA topoisomerase I	topA	
PA3012	9949114	hypothetical protein		
PA3017	9949120	conserved hypothetical protein		
PA3021	9949124	hypothetical protein		
PA3022	9949125	hypothetical protein		
PA3024	9949127	probable carbohydrate kinase		
PA3030	9949134	probable molybdopterin-guanine dinucleotide biosynthesis protein		mobA
PA3033	9949137	hypothetical protein		
PA3036	9949140	hypothetical protein		
PA3040	9949145	conserved hypothetical protein		yqjD
PA3041	9949146	hypothetical protein		yqjE
PA3042	9949147	hypothetical protein		
PA3046	9949151	conserved hypothetical protein		yggL
PA3049	9949155	ribosome modulation factor	rmf	
PA3051	9949157	hypothetical protein		
PA3067	9949174	probable transcriptional regulator		
PA3081	9949189	conserved hypothetical protein		
PA3085	9949193	hypothetical protein		
PA3088	9949197	conserved hypothetical protein		yfjB
PA3089	9949198	hypothetical protein		
PA3093	9949202	hypothetical protein		
PA3095	9949205	general secretion pathway protein M	xcpZ	
PA3096	9949206	general secretion pathway protein L	xcpY	
PA3100	9949210	general secretion pathway protein H	xcpU	pddB
PA3103	9949213	general secretion pathway protein E	xcpR	
PA3110	9949221	hypothetical protein		
PA3112	9949223	acetyl-CoA carboxylase beta subunit	accD	dedB
PA3117	9949229	aspartate semialdehyde dehydrogenase	asd	
PA3123	9949235	conserved hypothetical protein		
PA3140	9949254	hypothetical protein		
PA3142	9949256	hypothetical protein		
PA3144	9949258	hypothetical protein		
PA3145	9949259	glycosyltransferase WbpL	wbpL	
PA3146	9949260	probable NAD-dependent epimerase/dehydratase	wbpK	
PA3147	9949261	probable glycosyl transferase WbpJ	wbpJ	
PA3148	9949262	probable UDP-N-acetylglucosamine 2-epimerase	wbpI	
PA3149	9949263	probable glycosyltransferase WbpH	wbpH	
PA3150	9949264	LPS biosynthesis protein WbpG	wbpG	
PA3151	9949266	imidazoleglycerol-phosphate synthase, cyclase	hisF2	
PA3152	9949267	glutamine amidotransferase	hisH2	
PA3153	9949268	O-antigen translocase	wzx	wbpF, rfbX
PA3154	9949269	B-band O-antigen polymerase	wzy	rbc
PA3155	9949270	probable aminotransferase WbpE	wbpE	
PA3156	9949271	probable acetyltransferase WbpD	wbpD	
PA3157	9949272	probable acetyltransferase		wbpC
PA3158	9949273	probable oxidoreductase WbpB	wbpB	

PA3159	9949274	probable UDP-glucose/GDP-mannose dehydrogenase		
PA3160	9949276	O-antigen chain length regulator	wzz	cld, rol
PA3161	9949277	integration host factor beta subunit	himD	
PA3162	9949278	30S ribosomal protein S1	rpsA	
PA3163	9949279	cytidylate kinase	cmk	
PA3167	9949283	3-phosphoserine aminotransferase	serC	
PA3168	9949285	DNA gyrase subunit A	gyrA	
PA3171	9949288	3-demethylubiquinone-9 3-methyltransferase	ubiG	
PA3178	9949296	hypothetical protein		
PA3181	9949299	2-keto-3-deoxy-6-phosphogluconate aldolase		edaA
PA3185	9949303	hypothetical protein		
PA3195	9949314	glyceraldehyde 3-phosphate dehydrogenase	gapA	
PA3202	9949322	conserved hypothetical protein		ycil
PA3203	9949323	hypothetical protein		
PA3207	9949327	hypothetical protein		
PA3211	9949331	probable permease of ABC transporter		
PA3220	9949341	probable transcriptional regulator		
PA3227	9949348	peptidyl-prolyl cis-trans isomerase A	ppiA	cypH
PA3230	9949352	conserved hypothetical protein		
PA3232	9949354	probable nuclease		
PA3237	9949359	hypothetical protein		
PA3242	9949365	probable lauroyl acyltransferase		htrB
PA3245	9949368	cell division topological specificity factor MinE	minE	
PA3246	9949369	pseudouridine synthase RluA	rluA	yabO
PA3249	9949372	probable transcriptional regulator		
PA3255	9949379	hypothetical protein		
PA3260	9949384	probable transcriptional regulator		
PA3266	9949391	cold acclimation protein B	capB	cspA
PA3273	9949398	hypothetical protein		
PA3274	9949399	hypothetical protein		
PA3275	9949401	conserved hypothetical protein		ynfA
PA3278	9949404	hypothetical protein		
PA3280	9949406	outer membrane porin OprO precursor	oprO	
PA3281	9949407	hypothetical protein		
PA3287	9949414	conserved hypothetical protein		
PA3288	9949415	hypothetical protein		
PA3289	9949416	hypothetical protein		
PA3291	9949418	hypothetical protein		
PA3292	9949419	hypothetical protein		
PA3298	9949426	hypothetical protein		
PA3302	9949430	conserved hypothetical protein		
PA3309	9949438	conserved hypothetical protein		
PA3312	9949441	probable 3-hydroxyisobutyrate dehydrogenase		
PA3314	9949443	probable ATP-binding component of ABC trans		
PA3315	9949444	probable permease of ABC transporter		
PA3317	9949447	hypothetical protein		
PA3318	9949448	hypothetical protein		
PA3320	9949450	hypothetical protein		
PA3326	9949457	probable Clp-family ATP-dependent protease		
PA3330	9949461	probable short chain dehydrogenase		
PA3332	9949463	conserved hypothetical protein		
PA3334	9949465	probable acyl carrier protein		

PA3338	9949470	hypothetical protein		
PA3341	9949473	probable transcriptional regulator		
PA3347	9949480	hypothetical protein		
PA3348	9949481	probable chemotaxis protein methyltransferase		cheR1
PA3351	9949484	hypothetical protein		flgM
PA3353	9949486	hypothetical protein		
PA3354	9949487	hypothetical protein		
PA3360	9949494	probable secretion protein		
PA3367	9949502	hypothetical protein		ydcA
PA3368	9949503	probable acetyltransferase		
PA3370	9949505	hypothetical protein		
PA3371	9949506	hypothetical protein		
PA3380	9949515	conserved hypothetical protein		phnG
PA3384	9949519	ATP-binding component of ABC phosphonate	phnC	
PA3390	9949525	hypothetical protein		
PA3395	9949531	NosY protein	nosY	
PA3396	9949532	NosL protein	nosL	
PA3397	9949534	ferredoxin-NADP+ reductase	fpr	
PA3403	9949540	hypothetical protein		
PA3407	9949545	heme acquisition protein HasAp	hasAp	
PA3413	9949551	conserved hypothetical protein		yebG
PA3414	9949552	hypothetical protein		
PA3416	9949554	probable pyruvate dehydrogenase E1 compon		
PA3432	9949572	hypothetical protein		
PA3433	9949573	probable transcriptional regulator		ywbl
PA3434	9949574	probable transposase		
PA3435	9949575	conserved hypothetical protein		mioC
PA3438	9949578	GTP cyclohydrolase I precursor	folE1	
PA3439	9949579	d-erythro-7,8-dihydroneopterin triphosphate	folX	
PA3443	9949584	probable permease of ABC transporter		ssuC ycbM
PA3444	9949585	conserved hypothetical protein		ssuD
PA3445	9949586	conserved hypothetical protein		
PA3446	9949587	conserved hypothetical protein		ssuE
PA3450	9949591	probable antioxidant protein		lsfA
PA3451	9949592	hypothetical protein		
PA3460	9949602	probable acetyltransferase		
PA3470	9949614	hypothetical protein		
PA3472	9949616	hypothetical protein		
PA3477	9949621	transcriptional regulator RhIR	rhIR	
PA3482	9949627	methionyl-tRNA synthetase	metG	
PA3488	9949634	hypothetical protein		
PA3489	9949635	conserved hypothetical protein		rnfA
PA3492	9949638	conserved hypothetical protein		rnfD
PA3494	9949640	conserved hypothetical protein		rnfE
PA3495	9949641	endonuclease III	nth	
PA3496	9949642	hypothetical protein		
PA3501	9949647	hypothetical protein		
PA3502	9949648	hypothetical protein		
PA3505	9949652	hypothetical protein		
PA3512	9949659	probable permease of ABC transporter		
PA3519	9949667	hypothetical protein		
PA3520	9949668	hypothetical protein		

PA3523	9949671	probable RND efflux membrane fusion protein		
PA3528	9949677	ribonuclease T	rnt	
PA3530	9949679	conserved hypothetical protein		bfd
PA3533	9949682	conserved hypothetical protein		ydhD
PA3542	9949693	alginate biosynthesis protein Alg44		alg44
PA3550	9949702	alginate o-acetyltransferase AlgF	algF	
PA3558	9949710	hypothetical protein		
PA3566	9949719	conserved hypothetical protein		ycnE
PA3570	9949724	methylnalonate-semialdehyde dehydrogenase mmsA		
PA3572	9949726	hypothetical protein		
PA3575	9949729	hypothetical protein		
PA3578	9949732	conserved hypothetical protein		
PA3589	9949744	probable acyl-CoA thiolase		
PA3600	9949756	conserved hypothetical protein		rpl36
PA3601	9949757	conserved hypothetical protein		ykgM
PA3605	9949762	hypothetical protein		
PA3606	9949763	conserved hypothetical protein		yfiP
PA3609	9949766	polyamine transport protein PotC	potC	
PA3611	9949768	hypothetical protein		
PA3612	9949769	conserved hypothetical protein		ypeB
PA3616	9949774	conserved hypothetical protein		recX
PA3617	9949775	RecA protein	recA	
PA3627	9949785	conserved hypothetical protein		ygbB
PA3632	9949791	conserved hypothetical protein		yedF
PA3633	9949792	conserved hypothetical protein		ygbP
PA3634	9949793	conserved hypothetical protein		ybgQ
PA3635	9949794	enolase	eno	
PA3636	9949795	2-dehydro-3-deoxyphosphooctonate aldolase	kdsA	
PA3637	9949796	CTP synthase	pyrG	
PA3638	9949797	conserved hypothetical protein		mesJ
PA3639	9949798	acetyl-coenzyme A carboxylase carboxyl trans	accA	
PA3640	9949800	DNA polymerase III, alpha chain	dnaE	polC
PA3643	9949803	lipid A-disaccharide synthase	lpxB	pgsB
PA3644	9949804	UDP-N-acetylglucosamine acyltransferase	lpxA	
PA3645	9949805	(3R)-hydroxymyristoyl-[acyl carrier protein] dehyd	fabZ	sefA
PA3646	9949806	UDP-3-O-[3-hydroxylauroyl] glucosamine N-ac	lpxD	firA omsA
PA3647	9949807	probable outer membrane protein precursor		
PA3648	9949808	probable outer membrane protein		
PA3650	9949811	1-deoxy-d-xylulose 5-phosphate reductoisomerase	dxr	yaeM
PA3651	9949812	phosphatidate cytidyltransferase	cdsA	
PA3652	9949813	undecaprenyl pyrophosphate synthetase	uppS	yaeS
PA3653	9949814	ribosome recycling factor	frr	rrf
PA3654	9949815	uridylate kinase	pyrH	smbA
PA3655	9949816	elongation factor Ts	tsf	
PA3656	9949817	30S ribosomal protein S2	rpsB	
PA3657	9949818	methionine aminopeptidase	map	
PA3662	9949824	hypothetical protein		
PA3664	9949826	conserved hypothetical protein		yffB
PA3666	9949828	tetrahydrodipicolinate succinylase	dapD	
PA3671	9949833	probable permease of ABC transporter		
PA3674	9949837	hypothetical protein		
PA3678	9949841	probable transcriptional regulator		

PA3681	9949844	hypothetical protein		
PA3684	9949848	hypothetical protein		
PA3685	9949849	conserved hypothetical protein		
PA3688	9949852	hypothetical protein		
PA3693	9949858	conserved hypothetical protein		
PA3701		peptide chain release factor 2	prfB	
PA3704	9949868	probable chemotaxis sensor/effector fusion pro		
PA3719	9949885	hypothetical protein		
PA3725	9949891	single-stranded-DNA-specific exonuclease RetrecJ		
PA3726	9949892	conserved hypothetical protein		yaeQ
PA3730	9949897	hypothetical protein		
PA3731	9949898	conserved hypothetical protein		yjfJ
PA3733	9949900	hypothetical protein		
PA3742	9949910	50S ribosomal protein L19	rplS	
PA3743	9949911	tRNA (guanine-N1)-methyltransferase	trmD	
PA3744	9949912	16S rRNA processing protein	rimM	
PA3745	9949913	30S ribosomal protein S16	rpsP	
PA3746	9949914	signal recognition particle protein Ffh	ffh	
PA3752	9949921	hypothetical protein		
PA3754	9949923	hypothetical protein		yeaB
PA3756	9949925	hypothetical protein		yafK
PA3759	9949928	probable aminotransferase		
PA3765	9949935	hypothetical protein		
PA3767	9949937	conserved hypothetical protein		yfhC
PA3769	9949940	GMP synthase	guaA	
PA3773	9949944	hypothetical protein		
PA3776	9949947	probable transcriptional regulator		
PA3777	9949948	exodeoxyribonuclease VII large subunit	xseA	
PA3782	9949954	probable transcriptional regulator		
PA3784	9949956	hypothetical protein		
PA3785	9949957	conserved hypothetical protein		
PA3787	9949959	conserved hypothetical protein		
PA3788	9949960	hypothetical protein		
PA3796	9949969	hypothetical protein		
PA3800	9949973	conserved hypothetical protein		
PA3803	9949976	conserved hypothetical protein		gcpE
PA3805	9949978	type 4 fimbrial biogenesis protein PilF	pilF	
PA3806	9949979	conserved hypothetical protein		yfgB
PA3807	9949980	nucleoside diphosphate kinase	ndk	
PA3808	9949982	conserved hypothetical protein		yfhJ
PA3809	9949983	ferredoxin [2Fe-2S]	fdx2	
PA3810	9949984	heat shock protein HscA	hscA	
PA3811	9949985	heat shock protein HscB	hscB	
PA3812	9949986	probable iron-binding protein IscA	iscA	
PA3813	9949987	probable iron-binding protein IscU	iscU	
PA3815	9949989	conserved hypothetical protein		
PA3821	9949995	secretion protein SecD	secD	
PA3822	9949996	conserved hypothetical protein		yajC
PA3827	9950002	conserved hypothetical protein		yjgQ
PA3828	9950003	conserved hypothetical protein		yjgP
PA3829	9950004	hypothetical protein		
PA3833	9950008	hypothetical protein		

PA3834	9950009	valyl-tRNA synthetase	valS	
PA3835	9950010	hypothetical protein		
PA3840	9950016	conserved hypothetical protein		ybiN
PA3843	9950019	hypothetical protein		
PA3850	9950027	hypothetical protein		
PA3851	9950028	hypothetical protein		
PA3854	9950031	hypothetical protein		
PA3856	9950033	hypothetical protein		
PA3857	9950034	conserved hypothetical protein		
PA3859	9950037	probable carboxylesterase		
PA3867	9950046	probable DNA invertase		
PA3868	9950047	hypothetical protein		
PA3869	9950048	hypothetical protein		
PA3876	9950056	nitrite extrusion protein 2	nark2	
PA3884	9950064	hypothetical protein		
PA3886	9950066	hypothetical protein		
PA3888	9950069	probable permease of ABC transporter		
PA3890	9950071	probable permease of ABC transporter		
PA3891	9950072	probable ATP-binding component of ABC trans		
PA3892	9950073	conserved hypothetical protein		
PA3904	9950087	hypothetical protein		
PA3905	9950088	hypothetical protein		
PA3906	9950089	hypothetical protein		
PA3911	9950094	conserved hypothetical protein		yhbT
PA3916	9950100	molybdopterin converting factor, large subunit	moaE	
PA3917	9950101	molybdopterin converting factor, small subunit	moaD	
PA3918	9950102	molybdopterin biosynthetic protein C	moaC	
PA3936	9950122	probable permease of ABC taurine transporter		tauC
PA3940	9950127	probable DNA binding protein		
PA3960	9950149	hypothetical protein		
PA3962	9950151	hypothetical protein		
PA3965	9950154	probable transcriptional regulator		
PA3967	9950156	hypothetical protein		
PA3969	9950158	conserved hypothetical protein		
PA3973	9950163	probable transcriptional regulator		
PA3977	9950167	glutamate-1-semialdehyde 2,1-aminomutase	hemL	
PA3979	9950170	hypothetical protein		
PA3981	9950172	conserved hypothetical protein		ybeZ
PA3982	9950173	conserved hypothetical protein		
PA3984	9950175	apolipoprotein N-acyltransferase	Int	cutE
PA3986	9950177	hypothetical protein		
PA3987	9950178	leucyl-tRNA synthetase	leuS	
PA3988	9950179	hypothetical protein		
PA3989	9950180	DNA polymerase III, delta subunit	holA	
PA3990	9950182	conserved hypothetical protein		
PA3993	9950185	probable transposase		
PA3996	9950188	lipoate synthase	lipA	lip
PA3998	9950190	conserved hypothetical protein		ybeD
PA4002	9950194	rod shape-determining protein	rodA	mrdB
PA4005	9950197	conserved hypothetical protein		ybeB
PA4006	9950198	hypothetical protein		ybeN
PA4008	9950201	probable hydrolase		

PA4012	9950205	hypothetical protein		
PA4018	9950211	hypothetical protein		
PA4019	9950212	probable aromatic acid decarboxylase		
PA4028	9950222	hypothetical protein		
PA4029	9950224	conserved hypothetical protein		dedA
PA4031	9950226	inorganic pyrophosphatase	ppa	ipyR
PA4033	9950228	hypothetical protein		
PA4037	9950232	probable ATP-binding component of ABC trans		
PA4043	9950239	geranyltranstransferase	ispA	
PA4044	9950240	1-deoxyxylulose-5-phosphate synthase	dxs	
PA4047	9950243	GTP cyclohydrolase II	ribA	
PA4049	9950245	hypothetical protein		
PA4050	9950246	phosphatidylglycerophosphatase A	pgpA	
PA4051	9950247	thiamine monophosphate kinase	thiL	
PA4052	9950248	NusB protein	nusB	ssyB
PA4053	9950249	6,7-dimethyl-8-ribityllumazine synthase	ribE	ribH
PA4055	9950252	riboflavin synthase alpha chain	ribC	ribB
PA4056	9950253	riboflavin-specific deaminase/reductase	ribD	ribG
PA4057	9950254	conserved hypothetical protein		ybaD
PA4059	9950256	hypothetical protein		
PA4060	9950257	hypothetical protein		
PA4063	9950260	hypothetical protein		
PA4064	9950261	probable ATP-binding component of ABC trans		
PA4068	9950266	probable epimerase		
PA4076	9950274	hypothetical protein		
PA4077	9950275	probable transcriptional regulator		
PA4083	9950282	probable pili assembly chaperone		
PA4097	9950298	probable alcohol dehydrogenase (Zn-depende		ydjL
PA4099	9950300	hypothetical protein		
PA4104	9950305	conserved hypothetical protein		
PA4107	9950309	hypothetical protein		
PA4114	9950317	spermidine acetyltransferase		bltD
PA4121	9950324	conserved hypothetical protein		
PA4122	9950325	conserved hypothetical protein		
PA4125	9950329	5-carboxymethyl-2-hydroxymuconate isomerashpcD		
PA4134	9950339	hypothetical protein		
PA4141	9950346	hypothetical protein		
PA4149	9950355	conserved hypothetical protein		acoX
PA4151	9950357	acetoin catabolism protein AcoB	acoB	
PA4157	9950364	probable transcriptional regulator		
PA4164	9950372	hypothetical protein		
PA4167	9950375	probable oxidoreductase		yafB
PA4169	9950377	conserved hypothetical protein		
PA4170	9950378	hypothetical protein		
PA4171	9950379	probable protease		
PA4174	9950383	probable transcriptional regulator		
PA4176	9950385	peptidyl-prolyl cis-trans isomerase C2	ppiC2	
PA4181	9950390	hypothetical protein		
PA4182	9950391	hypothetical protein		
PA4183	9950392	hypothetical protein		
PA4190	9950400	probable FAD-dependent monooxygenase		
PA4209	9950421	probable O-methyltransferase		

PA4210	9950423	probable phenazine biosynthesis protein		phzA1
PA4211	9950424	probable phenazine biosynthesis protein		phzB1
PA4212	9950425	phenazine biosynthesis protein PhzC		phzC1
PA4215	9950428	probable phenazine biosynthesis protein		phzF1
PA4216	9950430	probable pyridoxamine 5'-phosphate oxidase		phzG1
PA4219	9950433	hypothetical protein		yfpB
PA4230	9950446	salicylate biosynthesis protein PchB	pchB	
PA4232	9950448	single-stranded DNA-binding protein	ssb	
PA4237	9950454	50S ribosomal protein L17	rplQ	
PA4238	9950455	DNA-directed RNA polymerase alpha chain	rpoA	
PA4239	9950456	30S ribosomal protein S4	rpsD	
PA4240	9950457	30S ribosomal protein S11	rpsK	
PA4241	9950458	30S ribosomal protein S13	rpsM	
PA4242	9950459	50S ribosomal protein L36	rpmJ	
PA4243	9950460	secretion protein SecY	secY	prlA
PA4244	9950461	50S ribosomal protein L15	rplO	
PA4245	9950462	50S ribosomal protein L30	rpmD	
PA4246	9950463	30S ribosomal protein S5	rpsE	
PA4247	9950464	50S ribosomal protein L18	rplR	
PA4248	9950465	50S ribosomal protein L6	rplF	
PA4249	9950466	30S ribosomal protein S8	rpsH	
PA4250	9950467	30S ribosomal protein S14	rpsN	
PA4251	9950468	50S ribosomal protein L5	rplE	
PA4252	9950469	50S ribosomal protein L24	rplX	
PA4253	9950470	50S ribosomal protein L14	rplN	
PA4254	9950471	30S ribosomal protein S17	rpsQ	
PA4255	9950472	50S ribosomal protein L29	rpmC	
PA4256	9950473	50S ribosomal protein L16	rplP	
PA4257	9950474	30S ribosomal protein S3	rpsC	
PA4258	9950475	50S ribosomal protein L22	rplV	
PA4259	9950476	30S ribosomal protein S19	rpsS	
PA4260	9950477	50S ribosomal protein L2	rplB	
PA4261	9950478	50S ribosomal protein L23	rplW	
PA4262	9950479	50S ribosomal protein L4	rplD	
PA4263	9950480	50S ribosomal protein L3	rplC	
PA4264	9950482	30S ribosomal protein S10	rpsJ	
PA4267	9950485	30S ribosomal protein S7	rpsG	
PA4268	9950486	30S ribosomal protein S12	rpsL	str
PA4269	9950487	DNA-directed RNA polymerase beta* chain	rpoC	
PA4270	9950488	DNA-directed RNA polymerase beta chain	rpoB	
PA4271	9950490	50S ribosomal protein L7 / L12	rplL	
PA4272	9950491	50S ribosomal protein L10	rplJ	
PA4273	9950492	50S ribosomal protein L1	rplA	
PA4274	9950493	50S ribosomal protein L11	rplK	
PA4275	9950494	transcription antitermination protein NusG	nusG	
PA4276	9950495	secretion protein SecE	secE	prlG
PA4279	9950498	hypothetical protein		
PA4295	9950516	hypothetical protein		
PA4296	9950518	probable two-component response regulator		
PA4298	9950520	hypothetical protein		
PA4299	9950521	hypothetical protein		
PA4305	9950527	hypothetical protein		

PA4306	9950529	hypothetical protein		
PA4314	9950538	formyltetrahydrofolate deformylase	purU1	
PA4322	9950546	conserved hypothetical protein		
PA4324	9950548	hypothetical protein		
PA4329	9950554	pyruvate kinase II	pykA	pyk-II
PA4330	9950555	probable enoyl-CoA hydratase/isomerase		
PA4341	9950567	probable transcriptional regulator		
PA4345	9950572	hypothetical protein		
PA4348	9950575	conserved hypothetical protein		
PA4349	9950576	hypothetical protein		
PA4350	9950577	conserved hypothetical protein		
PA4354	9950581	conserved hypothetical protein		
PA4357	9950584	conserved hypothetical protein		yhgG
PA4359	9950586	conserved hypothetical protein		feoA
PA4366	9950594	superoxide dismutase	sodB	
PA4373	9950602	hypothetical protein		
PA4377	9950607	hypothetical protein		
PA4383	9950613	conserved hypothetical protein		crcB
PA4385	9950615	GroEL protein	groEL	mopA
PA4386	9950616	GroES protein	groES	mopB
PA4388	9950618	hypothetical protein		
PA4389	9950619	probable short-chain dehydrogenase		
PA4392	9950623	conserved hypothetical protein		ybaZ
PA4395	9950626	conserved hypothetical protein		yajQ
PA4403	9950635	secretion protein SecA	secA	
PA4405	9950637	hypothetical protein		
PA4406	9950638	UDP-3-O-acetyl-N-acetylglucosamine deacetylase	spxC	envA asmB
PA4407	9950639	cell division protein FtsZ	ftsZ	
PA4408	9950640	cell division protein FtsA	ftsA	
PA4409	9950641	cell division protein FtsQ	ftsQ	
PA4411	9950643	UDP-N-acetylmuramate--alanine ligase	murC	
PA4412	9950644	UDP-N-acetylglucosamine--N-acetylmuramyl-6-phosphate transferase	ftsW	
PA4413	9950645	cell division protein FtsW	ftsW	
PA4414	9950646	UDP-N-acetylmuramoylalanine--D-glutamate transferase	ftsL	
PA4415	9950647	phospho-N-acetylmuramoyl-pentapeptide transferase	mraY	ORF Y
PA4416	9950648	UDP-N-acetylmuramoylalanine-D-glutamyl-2, 6-bisphosphate transferase	murF	
PA4417	9950649	UDP-N-acetylmuramoylalanine-D-glutamate-2, 6-bisphosphate transferase	murE	
PA4418	9950650	penicillin-binding protein 3	ftsI	pbpB
PA4419	9950651	cell division protein FtsL	ftsL	
PA4420	9950652	conserved hypothetical protein		mraW yabC ylxA
PA4421	9950653	conserved hypothetical protein		yabB
PA4424	9950657	conserved hypothetical protein		yraN
PA4425	9950658	probable phosphoheptose isomerase		yraO
PA4427	9950660	stringent starvation protein B	sspB	
PA4428	9950661	stringent starvation protein A	sspA	ssp pog
PA4430	9950663	probable cytochrome b		
PA4432	9950665	30S ribosomal protein S9	rpsI	
PA4433	9950666	50S ribosomal protein L13	rplM	
PA4436	9950670	probable transcriptional regulator		
PA4438	9950672	conserved hypothetical protein		yhcM
PA4439	9950673	tryptophanyl-tRNA synthetase	trpS	
PA4440	9950674	hypothetical protein		

PA4450	9950685	UDP-N-acetylglucosamine 1-carboxyvinyltrans	murA	
PA4452	9950687	conserved hypothetical protein		
PA4453	9950688	conserved hypothetical protein		
PA4454	9950689	conserved hypothetical protein		yrbD
PA4455	9950690	probable permease of ABC transporter		yrbE
PA4457	9950693	conserved hypothetical protein		yrbH kpsF
PA4459	9950695	conserved hypothetical protein		yrbK
PA4460	9950696	conserved hypothetical protein		yhbN
PA4461	9950697	probable ATP-binding component of ABC trans		yhbG
PA4462	9950698	RNA polymerase sigma-54 factor	rpoN	ntrA
PA4463	9950699	conserved hypothetical protein		yhbH
PA4464	9950700	nitrogen regulatory IIA protein	ptsN	
PA4466	9950702	probable phosphoryl carrier protein		
PA4471	9950707	hypothetical protein		fagA
PA4480	9950718	rod shape-determining protein MreC	mreC	
PA4481	9950719	rod shape-determining protein MreB	mreB	envB rodY
PA4482	9950720	Glu-tRNA(Gln) amidotransferase subunit C	gatC	
PA4483	9950721	Glu-tRNA(Gln) amidotransferase subunit A	gatA	
PA4484	9950722	Glu-tRNA(Gln) amidotransferase subunit B	gatB	
PA4485	9950723	conserved hypothetical protein		
PA4492	9950730	conserved hypothetical protein		
PA4499	9950738	probable transcriptional regulator		
PA4507	9950747	hypothetical protein		
PA4524	9950766	nicotinate-nucleotide pyrophosphorylase	nadC	
PA4525	9950767	type 4 fimbrial precursor PilA	pilA	
PA4526	9950768	type 4 fimbrial biogenesis protein PilB	pilB	
PA4527	9950770	still frameshift type 4 fimbrial biogenesis protei	pilC	
PA4529	9950772	conserved hypothetical protein		
PA4530	9950773	conserved hypothetical protein		
PA4537	9950780	hypothetical protein		
PA4544	9950788	pseudouridine synthase	rluD	yfiI
PA4547	9950791	two-component response regulator PilR	pilR	
PA4552	9950797	type 4 fimbrial biogenesis protein PilW	pilW	
PA4553	9950798	type 4 fimbrial biogenesis protein PilX	pilX	
PA4557	9950802	LytB protein	lytB	
PA4559	9950804	prolipoprotein signal peptidase	lspA	
PA4560	9950805	isoleucyl-tRNA synthetase	ileS	
PA4561	9950806	riboflavin kinase/FAD synthase	ribF	
PA4563	9950809	30S ribosomal protein S20	rpsT	
PA4564	9950810	conserved hypothetical protein		creA
PA4565	9950811	glutamate 5-kinase	proB	
PA4566	9950812	GTP-binding protein Obg	obg	
PA4567	9950813	50S ribosomal protein L27	rpmA	
PA4568	9950814	50S ribosomal protein L21	rplU	
PA4569	9950815	octaprenyl-diphosphate synthase	ispB	cel
PA4574	9950821	conserved hypothetical protein		yqhA
PA4575	9950822	hypothetical protein		
PA4577	9950824	hypothetical protein		
PA4586	9950834	hypothetical protein		
PA4600	9950850	transcriptional regulator NfxB	nfxB	
PA4603	9950853	hypothetical protein		
PA4610	9950861	hypothetical protein		

PA4611	9950862	hypothetical protein		
PA4617	9950868	conserved hypothetical protein		ygjO
PA4630	9950883	hypothetical protein		
PA4636	9950890	hypothetical protein		
PA4637	9950891	hypothetical protein		
PA4638	9950892	hypothetical protein		
PA4642	9950895	hypothetical protein		
PA4644	9950897	hypothetical protein		
PA4646	9950899	uracil phosphoribosyltransferase	upp	
PA4649	9950903	hypothetical protein		
PA4651	9950905	probable pill assembly chaperone		
PA4655	9950909	ferrochelatase	hemH	visA
PA4662	9950917	glutamate racemase	murl	
PA4663	9950918	molybdopterin biosynthesis MoeB protein	moeB	chIN
PA4665	9950920	peptide chain release factor 1	prfA	rf1
PA4666	9950921	glutamyl-tRNA reductase	hemA	hem1; glutR
PA4668	9950923	probable lipoprotein localization protein LolB		lolB
PA4669	9950924	isopentenyl monophosphate kinase	ipk	ychB
PA4670	9950925	ribose-phosphate pyrophosphokinase	prs	prsA
PA4671	9950927	probable ribosomal protein L25		rplY
PA4672	9950928	peptidyl-tRNA hydrolase		pth
PA4674	9950930	conserved hypothetical protein		vapl
PA4676	9950932	probable carbonic anhydrase		yadF
PA4679	9950935	hypothetical protein		
PA4681	9950937	hypothetical protein		
PA4693	9950950	phosphatidylserine synthase	pssA	
PA4696	9950953	acetolactate synthase large subunit	ilvI	
PA4697	9950955	hypothetical protein		
PA4698	9950956	hypothetical protein		yqcC
PA4699	9950957	hypothetical protein		
PA4702	9950960	hypothetical protein		
PA4706	9950964	probable ATP-binding component of ABC trans		phuV
PA4711	9950970	hypothetical protein		
PA4718	9950977	hypothetical protein		
PA4728	9950988	2-amino-4-hydroxy-6-hydroxymethyldihydropter	folK	
PA4729	9950989	3-methyl-2-oxobutanoate hydroxymethyltransf	panB	
PA4731	9950992	aspartate 1-decarboxylase precursor	panD	
PA4732	9950993	glucose-6-phosphate isomerase	pgi	
PA4737	9950998	hypothetical protein		
PA4738	9950999	conserved hypothetical protein		yjbJ
PA4739	9951000	conserved hypothetical protein		
PA4740	9951002	polyribonucleotide nucleotidyltransferase	pnp	
PA4741	9951003	30S ribosomal protein S15	rpsO	
PA4744	9951006	translation initiation factor IF-2'	infB	
PA4745	9951007	N utilization substance protein A	nusA	
PA4746	9951008	conserved hypothetical protein		yhbC
PA4747	9951009	secretion protein SecG	secG	
PA4748	9951010	triosephosphate isomerase	tpiA	tpi
PA4749	9951011	phosphoglucosamine mutase	glmM	yhbF, mrsA
PA4750	9951012	dihydropteroate synthase	folP	dhpS
PA4752	9951015	cell division protein FtsJ	ftsJ	
PA4753	9951016	conserved hypothetical protein		yhbY

PA4757	9951020	conserved hypothetical protein		yeaS
PA4759	9951022	dihydrodipicolinate reductase	dapB	
PA4762	9951026	heat shock protein GrpE	grpE	
PA4764	9951028	ferric uptake regulation protein	fur	
PA4765	9951029	outer membrane lipoprotein OmlA	omlA	oprX
PA4767	9951031	conserved hypothetical protein		yfjG
PA4773	9951038	hypothetical protein		
PA4776	9951041	probable two-component response regulator		
PA4778	9951043	probable transcriptional regulator		ybbI
PA4782	9951047	hypothetical protein		
PA4788	9951054	hypothetical protein		
PA4789	9951055	conserved hypothetical protein		
PA4790	9951056	conserved hypothetical protein		smtA
PA4792	9951058	conserved hypothetical protein		
PA4797	9951064	probable transposase		
PA4802	9951069	hypothetical protein		
PA4809	9951077	FdhE protein	fdhE	
PA4813	9951080	lipase LipC	lipC	
PA4823	9951091	hypothetical protein		
PA4826	9951095	hypothetical protein		
PA4828	9951097	conserved hypothetical protein		
PA4831	9951100	probable transcriptional regulator		
PA4841	9951111	conserved hypothetical protein		
PA4847	9951118	biotin carboxyl carrier protein (BCCP)	accB	fabE
PA4848	9951119	biotin carboxylase	accC	
PA4850	9951121	ribosomal protein L11 methyltransferase	prmA	
PA4853	9951124	DNA-binding protein Fis	fis	
PA4861	9951133	probable ATP-binding component of ABC trans		
PA4864	9951137	urease accessory protein	ureD	
PA4866	9951139	conserved hypothetical protein		
PA4868	9951141	urease alpha subunit	ureC	
PA4870	9951143	conserved hypothetical protein		ybil
PA4871	9951144	hypothetical protein		
PA4874	9951148	conserved hypothetical protein		psiF
PA4875	9951149	hypothetical protein		
PA4878	9951152	probable transcriptional regulator		
PA4885	9951159	two-component response regulator	irlR	
PA4887	9951161	probable MFS transporter		
PA4890	9951165	conserved hypothetical protein		yijC
PA4892	9951167	urease accessory protein UreF	ureF	
PA4894	9951169	hypothetical protein		
PA4895	9951170	probable transmembrane sensor		
PA4906	9951182	probable transcriptional regulator		
PA4908	9951185	hypothetical protein		
PA4916	9951193	hypothetical protein		
PA4920	9951198	NH ₃ -dependent NAD synthetase	nadE	
PA4923	9951201	conserved hypothetical protein		
PA4925	9951203	conserved hypothetical protein		
PA4926	9951204	conserved hypothetical protein		
PA4931	9951210	replicative DNA helicase	dnaB	
PA4934	9951213	30S ribosomal protein S18	rpsR	
PA4935	9951214	30S ribosomal protein S6	rpsF	

PA4938	9951218	adenylosuccinate synthetase	purA	
PA4940	9951220	conserved hypothetical protein		yjeT
PA4944	9951224	conserved hypothetical protein		hfq
PA4945	9951225	delta 2-isopentenylpyrophosphate transferase	miaA	
PA4948	9951228	conserved hypothetical protein		yjeE
PA4952	9951233	conserved hypothetical protein		yjeQ
PA4956	9951237	thiosulfate sulfurtransferase	rhdA	
PA4961	9951243	hypothetical protein		
PA4962	9951244	conserved hypothetical protein		ybcI
PA4964	9951246	topoisomerase IV subunit A	parC	
PA4965	9951247	hypothetical protein		
PA4966	9951248	hypothetical protein		
PA4967	9951249	topoisomerase IV subunit B	parE	
PA4969	9951252	conserved hypothetical protein		icc
PA4972	9951255	hypothetical protein		
PA4980	9951263	probable enoyl-CoA hydratase/isomerase		
PA4988	9951272	3-deoxy-D-manno-octulosonic-acid (KDO) transferase	waaA	kdtA
PA4990	9951275	SMR multidrug efflux transporter		
PA4991	9951276	hypothetical protein		
PA4992	9951277	hypothetical protein		
PA4997	9951282	transport protein MsbA	msbA	
PA4998	9951283	conserved hypothetical protein		
PA5006	9951292	hypothetical protein		
PA5007	9951293	hypothetical protein		wapQ inaA
PA5008	9951294	hypothetical protein		wapP waaX
PA5009	9951295	lipopolysaccharide core biosynthesis protein V	waaP	rfaP
PA5010	9951296	UDP-glucose:(heptosyl) LPS alpha 1,3-glucosyltransferase	waaG	rfaG
PA5011	9951297	heptosyltransferase I	waaC	rfaC
PA5012	9951298	heptosyltransferase II	waaF	rfaF
PA5028	9951317	conserved hypothetical protein		
PA5032	9951321	probable transcriptional regulator		
PA5033	9951322	hypothetical protein		
PA5034	9951323	uroporphyrinogen decarboxylase	hemE	
PA5039	9951329	shikimate kinase	aroK	
PA5044	9951334	type 4 fimbrial biogenesis protein PilM	pilM	
PA5050	9951341	primosomal protein N'	priA	
PA5051	9951342	arginyl-tRNA synthetase	argS	
PA5052	9951343	hypothetical protein		
PA5061	9951353	conserved hypothetical protein		phal
PA5063	9951355	ubiquinone biosynthesis methyltransferase	ubiE	
PA5064	9951356	hypothetical protein		
PA5065	9951357	conserved hypothetical protein		aarF yigR
PA5067	9951360	phosphoribosyl-ATP pyrophosphohydrolase	hisE	
PA5068	9951361	translocation protein Tata	tatA	mttA yigT
PA5071	9951364	conserved hypothetical protein		
PA5072	9951365	probable chemotaxis transducer		
PA5081	9951375	hypothetical protein		
PA5085	9951379	probable transcriptional regulator		
PA5110	9951406	fructose-1,6-bisphosphatase	fbp	cbbF, cfxF
PA5111	9951408	lactoylglutathione lyase	gloA3	glo1
PA5116	9951413	probable transcriptional regulator		
PA5119	9951417	glutamine synthetase	glnA	

PA5128	9951427	secretion protein SecB	secB	
PA5129	9951428	glutaredoxin	grx	
PA5130	9951429	conserved hypothetical protein		yibN
PA5131	9951430	phosphoglycerate mutase	pgm	yibO
PA5132	9951431	hypothetical protein		
PA5142	9951442	glutamine amidotransferase	hisH1	
PA5144	9951444	hypothetical protein		
PA5148	9951448	conserved hypothetical protein		yggX
PA5154	9951455	probable permease of ABC transporter		
PA5161	9951463	dTDP-D-glucose 4,6-dehydratase	rmlB	rfbB
PA5162	9951464	dTDP-4-dehydrorhamnose reductase	rmlD	rfbD
PA5163	9951465	glucose-1-phosphate thymidyltransferase	rmlA	rfbA
PA5164	9951466	dTDP-4-dehydrorhamnose 3,5-epimerase	rmlC	rfbC
PA5173	9951476	carbamate kinase	arcC	
PA5176	9951479	conserved hypothetical protein		yrfE
PA5178	9951481	conserved hypothetical protein		
PA5182	9951486	hypothetical protein		
PA5187	9951491	probable acyl-CoA dehydrogenase		
PA5190	9951495	probable nitroreductase		
PA5195	9951500	probable heat shock protein		yrfH
PA5221	9951529	probable FAD-dependent monooxygenase		visC
PA5222	9951530	hypothetical protein		
PA5224	9951532	aminopeptidase P	pepP	
PA5225	9951533	hypothetical protein		
PA5227	9951535	conserved hypothetical protein		ygfE
PA5229	9951537	conserved hypothetical protein		
PA5237	9951546	conserved hypothetical protein		yigC
PA5239	9951548	transcription termination factor Rho	rho	
PA5240	9951549	thioredoxin	trxA	
PA5246	9951556	conserved hypothetical protein		yigI
PA5247	9951557	conserved hypothetical protein		yail
PA5259	9951570	uroporphyrinogen-III synthetase	hemD	
PA5260	9951571	porphobilinogen deaminase	hemC	popE
PA5275	9951588	conserved hypothetical protein		cyaY
PA5276	9951589	lipopeptide LppL precursor	lppL	
PA5278	9951591	diaminopimelate epimerase	dapF	
PA5281	9951594	probable hydrolase		yigB
PA5288	9951602	nitrogen regulatory protein P-II 2	glnK	
PA5296	9951611	ATP-dependent DNA helicase Rep	rep	
PA5300	9951616	cytochrome c5	cycB	
PA5303	9951619	conserved hypothetical protein		
PA5316	9951633	50S ribosomal protein L28	rpmB	
PA5319	9951636	DNA repair protein RadC	radC	
PA5320	9951637	DNA/pantothenate metabolism flavoprotein	dfp	
PA5321	9951638	deoxyuridine 5'-triphosphate nucleotidohydrolase	dut	
PA5325	9951643	hypothetical protein		
PA5328	9951646	probable cytochrome c(mono-heme type)		
PA5330	9951648	hypothetical protein		
PA5331	9951649	orotate phosphoribosyltransferase	pyrE	
PA5333	9951652	conserved hypothetical protein		
PA5334	9951653	ribonuclease PH	rph	
PA5335	9951654	conserved hypothetical protein		yicC

PA5336	9951655	guanylate kinase	gmk	
PA5339	9951658	conserved hypothetical protein		
PA5347	9951667	hypothetical protein		
PA5350	9951670	rubredoxin		
PA5351	9951671	rubredoxin		
PA5358	9951678	4-hydroxybenzoate-octaprenyl transferase	ubiA	
PA5364	9951685	probable two-component response regulator		
PA5381	9951704	hypothetical protein		
PA5385	9951709	hypothetical protein		
PA5390	9951714	probable peptidic bond hydrolase		
PA5396	9951721	hypothetical protein		
PA5403	9951729	probable transcriptional regulator		
PA5404	9951730	hypothetical protein		
PA5406	9951732	hypothetical protein		
PA5408	9951734	hypothetical protein		
PA5417	9951744	sarcosine oxidase delta subunit	soxD	
PA5457	9951788	hypothetical protein		
PA5460	9951792	hypothetical protein		
PA5465	9951797	hypothetical protein		
PA5469	9951801	conserved hypothetical protein		
PA5470	9951802	probable peptide chain release factor		prfH
PA5480	9951813	hypothetical protein		
PA5482	9951816	hypothetical protein		
PA5496	9951831	hypothetical protein		
PA5503	9951839	probable ATP-binding component of ABC trans		
PA5526	9951864	hypothetical protein		
PA5529	9951867	probable sodium/proton antiporter		
PA5531	9951869	TonB protein	tonB	
PA5533	9951871	hypothetical protein		
PA5534	9951873	hypothetical protein		
PA5543	9951882	hypothetical protein		
PA5549	9951889	glucosamine--fructose-6-phosphate aminotran	glmS	
PA5552	9951892	glucosamine-1-phosphate acetyltransferase/N	glmU	gcaD
PA5553	9951893	ATP synthase epsilon chain	atpC	uncC papG
PA5554	9951894	ATP synthase beta chain	atpD	uncD papB
PA5555	9951895	ATP synthase gamma chain	atpG	uncG papC
PA5556	9951896	ATP synthase alpha chain	atpA	uncA papA
PA5557	9951897	ATP synthase delta chain	atpH	uncH papE
PA5558	9951898	ATP synthase B chain	atpF	uncF papF
PA5559	9951899	atp synthase C chain	atpE	uncE papH
PA5560	9951900	ATP synthase A chain	atpB	uncB papD
PA5561	9951901	ATP synthase protein I	atpI	uncI
PA5562	9951903	chromosome partitioning protein Spo0J	spo0J	
PA5566	9951907	hypothetical protein		
PA5568	9951909	conserved hypothetical protein		yidC
PA5569	9951910	ribonuclease P protein component	mpA	
PA5570	9951911	50S ribosomal protein L34	rpmH	

Primary Function	Range From	Range To
DNA replication, recombination, modification	483	2027
DNA replication, recombination, modification	4275	6695
Hypothetical, unclassified, unknown	8339	7803
Translation, post-translational modification	12488	10434
Translation, post-translational modification	13435	12488
Cell wall / LPS / capsule	14235	15122
Hypothetical, unclassified, unknown	17217	16900
Hypothetical, unclassified, unknown	24001	24558
Hypothetical, unclassified, unknown	27646	28632
Hypothetical, unclassified, unknown	36270	35905
Amino acid biosynthesis and metabolism	37893	37087
Hypothetical, unclassified, unknown	40190	40405
Hypothetical, unclassified, unknown	40589	40816
Hypothetical, unclassified, unknown	56546	56941
Hypothetical, unclassified, unknown	61879	62388
Hypothetical, unclassified, unknown	68616	68188
Hypothetical, unclassified, unknown	69272	69526
Hypothetical, unclassified, unknown	70091	69543
Hypothetical, unclassified, unknown	70636	70130
Hypothetical, unclassified, unknown	72680	73384
Adaptation, protection	73468	73923
Hypothetical, unclassified, unknown	74034	74267
Hypothetical, unclassified, unknown	74716	74279
Hypothetical, unclassified, unknown	78097	77432
Hypothetical, unclassified, unknown	80752	81027
Hypothetical, unclassified, unknown	81116	82174
Hypothetical, unclassified, unknown	83318	82404
Hypothetical, unclassified, unknown	98218	97754
Hypothetical, unclassified, unknown	100124	101158
Hypothetical, unclassified, unknown	115045	114611
Hypothetical, unclassified, unknown	119127	120164
Hypothetical, unclassified, unknown	121346	122266
Energy metabolism	127378	128502
Hypothetical, unclassified, unknown	131792	131583
Hypothetical, unclassified, unknown	132577	133155
Energy metabolism	134319	135233
Hypothetical, unclassified, unknown	135259	135894
Hypothetical, unclassified, unknown	136386	135934
Hypothetical, unclassified, unknown	136518	136991
Transport of small molecules	138818	140167
Transcriptional regulators	140216	140902
Hypothetical, unclassified, unknown	143848	143567
Hypothetical, unclassified, unknown	144072	143845
Hypothetical, unclassified, unknown	145542	145883
Hypothetical, unclassified, unknown	149425	149138
Transcriptional regulators	150906	151823
Hypothetical, unclassified, unknown	153696	153836
Adaptation, protection	158199	158762
Nucleotide biosynthesis and metabolism	163426	164415
Hypothetical, unclassified, unknown	165737	165219
Transcriptional regulators	169361	169906

Carbon compound catabolism	175503	176108
Transcriptional regulators	182768	183706
Hypothetical, unclassified, unknown	184287	184439
Transcriptional regulators	191697	192362
Hypothetical, unclassified, unknown	194179	193799
Hypothetical, unclassified, unknown	194748	194206
Putative enzymes	207071	207823
Carbon compound catabolism	209533	207923
Transport of small molecules	210460	209621
Hypothetical, unclassified, unknown	213819	214634
Hypothetical, unclassified, unknown	214631	215512
Hypothetical, unclassified, unknown	229738	229526
Putative enzymes	232000	230543
Transport of small molecules	233100	232066
Transport of small molecules	233932	233123
Transport of small molecules	234849	233929
Transcriptional regulators	236218	237111
Hypothetical, unclassified, unknown	238896	239777
Carbon compound catabolism	240071	240934
Hypothetical, unclassified, unknown	241753	242445
Transport of small molecules	243841	244605
Transcriptional regulators	262557	263498
Transcriptional regulators	266616	267395
Hypothetical, unclassified, unknown	268704	269519
Transcriptional regulators	275772	276440
Hypothetical, unclassified, unknown	277334	276480
Amino acid biosynthesis and metabolism	277777	277331
Hypothetical, unclassified, unknown	282757	282323
Hypothetical, unclassified, unknown	283553	282912
Hypothetical, unclassified, unknown	289390	289205
Hypothetical, unclassified, unknown	293304	291154
Hypothetical, unclassified, unknown	293798	293301
Hypothetical, unclassified, unknown	299497	299081
Transport of small molecules	309092	307878
Transcriptional regulators	313227	313925
Transport of small molecules	314927	313938
Hypothetical, unclassified, unknown	318148	317966
Hypothetical, unclassified, unknown	350841	350089
Hypothetical, unclassified, unknown	352164	351610
Hypothetical, unclassified, unknown	359982	360332
Energy metabolism	371833	371162
Hypothetical, unclassified, unknown	373725	374192
Hypothetical, unclassified, unknown	378096	378575
Hypothetical, unclassified, unknown	382792	382037
Fatty acid and phospholipid metabolism	383727	384527
Nucleotide biosynthesis and metabolism	384733	385527
Biosynthesis of cofactors, prosthetic group	393308	393814
Hypothetical, unclassified, unknown	402020	402598
Energy metabolism	406498	406247
Central intermediary metabolism	407098	406619
Hypothetical, unclassified, unknown	413654	413364
Hypothetical, unclassified, unknown	414529	413933

Protein secretion/export apparatus	417527	418894
Transcriptional regulators	420683	421537
Hypothetical, unclassified, unknown	421602	422207
Hypothetical, unclassified, unknown	423460	423660
Hypothetical, unclassified, unknown	427120	426863
Hypothetical, unclassified, unknown	439991	440395
Nucleotide biosynthesis and metabolism	445691	444687
Transcriptional regulators	446227	445715
Hypothetical, unclassified, unknown	446773	446339
Hypothetical, unclassified, unknown	447342	446773
Biosynthesis of cofactors, prosthetic grou	449384	448431
Motility & Attachment	453239	454114
Transcriptional regulators	463079	463873
Hypothetical, unclassified, unknown	470081	470650
Transport of small molecules	476333	477790
Hypothetical, unclassified, unknown	484404	484838
Hypothetical, unclassified, unknown	496478	496362
Transport of small molecules	496871	498361
Related to phage, transposon, or plasmid	501120	500104
Hypothetical, unclassified, unknown	502599	501376
Transcriptional regulators	504121	505029
Hypothetical, unclassified, unknown	510499	509825
Adaptation, protection	514775	514984
Hypothetical, unclassified, unknown	526877	527179
Hypothetical, unclassified, unknown	535085	535489
Transcriptional regulators	535539	536108
Transcriptional regulators	539143	538217
Transcriptional regulators	540735	539785
Hypothetical, unclassified, unknown	549614	549294
Putative enzymes	550381	549656
Hypothetical, unclassified, unknown	550813	550520
Putative enzymes	552746	552994
Hypothetical, unclassified, unknown	558361	557354
Biosynthesis of cofactors, prosthetic grou	560808	562013
Biosynthesis of cofactors, prosthetic grou	562006	562728
Biosynthesis of cofactors, prosthetic grou	562721	563545
Biosynthesis of cofactors, prosthetic grou	563549	564235
Hypothetical, unclassified, unknown	564344	564574
Biosynthesis of cofactors, prosthetic grou	576040	575516
Transcriptional regulators	586663	585980
Putative enzymes	590105	590821
Transcriptional regulators	594580	595134
Hypothetical, unclassified, unknown	598608	598994
Hypothetical, unclassified, unknown	600176	599757
Hypothetical, unclassified, unknown	600426	601394
Hypothetical, unclassified, unknown	602141	601398
Central intermediary metabolism	604896	603706
Hypothetical, unclassified, unknown	609999	609202
Energy metabolism	611281	612444
Hypothetical, unclassified, unknown	612517	612717
Carbon compound catabolism	613338	614402
Hypothetical, unclassified, unknown	617549	616371

Hypothetical, unclassified, unknown	620488	620135
Hypothetical, unclassified, unknown	621695	622033
Hypothetical, unclassified, unknown	622726	622884
Hypothetical, unclassified, unknown	624199	623852
Hypothetical, unclassified, unknown	624803	624189
Hypothetical, unclassified, unknown	629884	628763
Hypothetical, unclassified, unknown	638830	638381
Translation, post-translational modification	639115	638900
Translation, post-translational modification	639316	640341
Biosynthesis of cofactors, prosthetic group	641073	641426
Hypothetical, unclassified, unknown	643714	643208
Hypothetical, unclassified, unknown	649263	648931
Hypothetical, unclassified, unknown	650538	650158
Biosynthesis of cofactors, prosthetic group	652483	651497
Chaperones & heat shock proteins	653772	652480
Adaptation, protection	656527	653753
Energy metabolism	669415	670089
Transcriptional regulators	673091	672777
Transcriptional regulators	673961	673191
Hypothetical, unclassified, unknown	674667	675026
Hypothetical, unclassified, unknown	675390	675839
Related to phage, transposon, or plasmid	677083	677409
Hypothetical, unclassified, unknown	685846	686718
Hypothetical, unclassified, unknown	686693	686899
Related to phage, transposon, or plasmid	688605	688967
Related to phage, transposon, or plasmid	689236	689466
Related to phage, transposon, or plasmid	690420	690674
Hypothetical, unclassified, unknown	693596	694366
Hypothetical, unclassified, unknown	698932	699720
Hypothetical, unclassified, unknown	699744	700835
Related to phage, transposon, or plasmid	700835	701170
Hypothetical, unclassified, unknown	701477	702529
Related to phage, transposon, or plasmid	702529	702831
Related to phage, transposon, or plasmid	702828	703058
Transcriptional regulators	706672	706028
Hypothetical, unclassified, unknown	706944	707366
Hypothetical, unclassified, unknown	709182	708535
Hypothetical, unclassified, unknown	714247	713279
Hypothetical, unclassified, unknown	714686	714264
Hypothetical, unclassified, unknown	717231	717581
Protein secretion/export apparatus	737530	737081
Hypothetical, unclassified, unknown	737677	738108
Protein secretion/export apparatus	738485	738111
Protein secretion/export apparatus	741335	741928
Protein secretion/export apparatus	744333	745742
Protein secretion/export apparatus	745742	746956
Hypothetical, unclassified, unknown	748662	749774
Hypothetical, unclassified, unknown	770156	770818
Hypothetical, unclassified, unknown	770847	771326
Hypothetical, unclassified, unknown	772275	772700
Hypothetical, unclassified, unknown	775321	774416
Putative enzymes	778181	776787

Putative enzymes	779208	778309
Transcriptional regulators	782113	781259
Hypothetical, unclassified, unknown	782229	782525
Central intermediary metabolism	782570	782965
Hypothetical, unclassified, unknown	783833	783576
Hypothetical, unclassified, unknown	784698	785174
Hypothetical, unclassified, unknown	785969	786925
Hypothetical, unclassified, unknown	786928	788253
Related to phage, transposon, or plasmid	789144	789356
Related to phage, transposon, or plasmid	790166	790600
Related to phage, transposon, or plasmid	795793	796776
Hypothetical, unclassified, unknown	797251	797598
Putative enzymes	798827	797925
Transcription, RNA processing and degradation	801967	801275
Hypothetical, unclassified, unknown	802239	801967
Hypothetical, unclassified, unknown	805228	805473
Hypothetical, unclassified, unknown	809882	809574
Hypothetical, unclassified, unknown	828344	827400
Secreted Factors (toxins, enzymes, alginate)	831914	832498
Protein secretion/export apparatus	835523	837322
Protein secretion/export apparatus	837328	838182
Translation, post-translational modification	839407	840324
Hypothetical, unclassified, unknown	844295	843723
Hypothetical, unclassified, unknown	845682	845278
Transport of small molecules	858646	858951
Hypothetical, unclassified, unknown	859007	860170
Hypothetical, unclassified, unknown	866451	865636
Hypothetical, unclassified, unknown	881077	881400
Hypothetical, unclassified, unknown	883216	882989
Hypothetical, unclassified, unknown	885635	886108
Transcriptional regulators	893041	893994
Hypothetical, unclassified, unknown	895668	895396
Hypothetical, unclassified, unknown	896416	897228
Hypothetical, unclassified, unknown	898886	898440
Hypothetical, unclassified, unknown	900165	899830
Hypothetical, unclassified, unknown	901046	900408
Putative enzymes	903692	904633
Chaperones & heat shock proteins	913086	913571
Hypothetical, unclassified, unknown	929084	929503
Hypothetical, unclassified, unknown	930476	929514
Putative enzymes	932725	932102
Cell division	935989	936294
Hypothetical, unclassified, unknown	942648	943430
Hypothetical, unclassified, unknown	948776	949159
Hypothetical, unclassified, unknown	949280	949693
Cell wall / LPS / capsule	950648	949716
Amino acid biosynthesis and metabolism	952514	952158
Hypothetical, unclassified, unknown	955722	955456
Putative enzymes	962545	962925
Hypothetical, unclassified, unknown	977743	977420
Hypothetical, unclassified, unknown	984245	984535
Translation, post-translational modification	986818	989442

Amino acid biosynthesis and metabolism	989590	990828
Transcriptional regulators	991013	991198
Transcriptional regulators	992543	991830
Hypothetical, unclassified, unknown	993409	993783
Hypothetical, unclassified, unknown	993776	994051
Transport of small molecules	996038	997486
Hypothetical, unclassified, unknown	1007548	1007234
Carbon compound catabolism	1012972	1011983
Amino acid biosynthesis and metabolism	1020708	1021607
Hypothetical, unclassified, unknown	1027445	1027984
Hypothetical, unclassified, unknown	1030151	1029825
Nucleotide biosynthesis and metabolism	1032763	1032095
Nucleotide biosynthesis and metabolism	1033824	1032763
Hypothetical, unclassified, unknown	1035277	1035981
Putative enzymes	1039968	1040432
Putative enzymes	1040432	1040707
Translation, post-translational modification	1043404	1041689
Hypothetical, unclassified, unknown	1046462	1046671
Adaptation, protection	1048019	1047549
Transport of small molecules	1053848	1054543
Transport of small molecules	1054566	1055006
Transport of small molecules	1055009	1056052
Transport of small molecules	1056049	1057347
Transport of small molecules	1057400	1057906
Hypothetical, unclassified, unknown	1059622	1060296
Hypothetical, unclassified, unknown	1062034	1061207
Hypothetical, unclassified, unknown	1062369	1062061
Hypothetical, unclassified, unknown	1062601	1062885
Hypothetical, unclassified, unknown	1062921	1063544
Hypothetical, unclassified, unknown	1065138	1065425
Secreted Factors (toxins, enzymes, alginate)	1067817	1066321
Hypothetical, unclassified, unknown	1068193	1068456
Hypothetical, unclassified, unknown	1071877	1071239
Hypothetical, unclassified, unknown	1072462	1072839
Chaperones & heat shock proteins	1073960	1074673
Hypothetical, unclassified, unknown	1082949	1083854
Hypothetical, unclassified, unknown	1090606	1090857
Adaptation, protection	1092498	1092025
Amino acid biosynthesis and metabolism	1093251	1094129
Hypothetical, unclassified, unknown	1095276	1096034
Nucleotide biosynthesis and metabolism	1096063	1096773
Putative enzymes	1107000	1107761
Hypothetical, unclassified, unknown	1113050	1112574
Hypothetical, unclassified, unknown	1123850	1123356
Hypothetical, unclassified, unknown	1125865	1125548
Hypothetical, unclassified, unknown	1126338	1125865
Biosynthesis of cofactors, prosthetic groups	1136388	1137035
Hypothetical, unclassified, unknown	1144862	1145200
Hypothetical, unclassified, unknown	1150470	1150721
Chaperones & heat shock proteins	1153637	1155547
Hypothetical, unclassified, unknown	1163660	1164022
Hypothetical, unclassified, unknown	1175614	1176375

Hypothetical, unclassified, unknown	1176380	1176982
Hypothetical, unclassified, unknown	1176958	1177620
Hypothetical, unclassified, unknown	1186606	1186986
Two-component regulatory systems	1189172	1190380
Motility & Attachment	1194207	1195223
Motility & Attachment	1197390	1197833
Hypothetical, unclassified, unknown	1198551	1197838
Hypothetical, unclassified, unknown	1199946	1198750
Hypothetical, unclassified, unknown	1207875	1207540
Hypothetical, unclassified, unknown	1212571	1211888
Hypothetical, unclassified, unknown	1214502	1213195
Translation, post-translational modification	1215284	1215727
Biosynthesis of cofactors, prosthetic group	1218181	1218933
Antibiotic resistance and susceptibility	1221691	1222098
Hypothetical, unclassified, unknown	1226278	1225757
Hypothetical, unclassified, unknown	1227302	1226427
Transcriptional regulators	1229344	1230219
Transcriptional regulators	1236644	1237546
Hypothetical, unclassified, unknown	1243118	1242750
Adaptation, protection	1245665	1245928
Hypothetical, unclassified, unknown	1249552	1249019
Nucleotide biosynthesis and metabolism	1251154	1249907
Nucleotide biosynthesis and metabolism	1254309	1251418
Two-component regulatory systems	1255042	1255752
Adaptation, protection	1257772	1257981
Hypothetical, unclassified, unknown	1258470	1258087
Amino acid biosynthesis and metabolism	1260442	1259291
Hypothetical, unclassified, unknown	1263378	1264190
Hypothetical, unclassified, unknown	1264919	1264191
Hypothetical, unclassified, unknown	1266111	1266782
Hypothetical, unclassified, unknown	1267282	1267602
Energy metabolism	1272796	1272200
Energy metabolism	1273298	1272807
Energy metabolism	1276608	1276117
Energy metabolism	1276784	1276617
Transport of small molecules	1284513	1285823
Hypothetical, unclassified, unknown	1294138	1294809
Hypothetical, unclassified, unknown	1303457	1303864
Hypothetical, unclassified, unknown	1303892	1304449
Hypothetical, unclassified, unknown	1305583	1306056
Hypothetical, unclassified, unknown	1314321	1313362
Hypothetical, unclassified, unknown	1317202	1315916
Hypothetical, unclassified, unknown	1318150	1317404
Amino acid biosynthesis and metabolism	1319514	1318147
Hypothetical, unclassified, unknown	1321000	1320386
Transcriptional regulators	1326939	1326046
Putative enzymes	1327024	1327803
Hypothetical, unclassified, unknown	1330467	1330117
Hypothetical, unclassified, unknown	1331517	1331714
Hypothetical, unclassified, unknown	1334671	1334928
Antibiotic resistance and susceptibility	1339082	1337931
Secreted Factors (toxins, enzymes, alginate)	1357317	1357712

Transcriptional regulators	1370092	1369418
Transcriptional regulators	1379168	1378500
Hypothetical, unclassified, unknown	1391277	1391861
Transcriptional regulators	1396731	1397180
Hypothetical, unclassified, unknown	1406459	1406752
Hypothetical, unclassified, unknown	1408999	1409274
Transcriptional regulators	1409949	1410476
Putative enzymes	1417500	1417961
Hypothetical, unclassified, unknown	1417965	1418738
Transcriptional regulators	1425754	1425140
Energy metabolism	1432037	1432927
Hypothetical, unclassified, unknown	1435493	1435825
Transcriptional regulators	1441547	1440639
Hypothetical, unclassified, unknown	1444451	1442904
Transport of small molecules	1456723	1455815
Hypothetical, unclassified, unknown	1462696	1463403
Hypothetical, unclassified, unknown	1463586	1463936
Hypothetical, unclassified, unknown	1464111	1464860
Hypothetical, unclassified, unknown	1467320	1466109
Hypothetical, unclassified, unknown	1467901	1467488
Hypothetical, unclassified, unknown	1468510	1468890
Hypothetical, unclassified, unknown	1470978	1470580
Hypothetical, unclassified, unknown	1474391	1474714
Transcriptional regulators	1475464	1476306
Hypothetical, unclassified, unknown	1479791	1479021
Hypothetical, unclassified, unknown	1483123	1483875
Hypothetical, unclassified, unknown	1483898	1485763
Hypothetical, unclassified, unknown	1486967	1486266
Hypothetical, unclassified, unknown	1489095	1486960
Biosynthesis of cofactors, prosthetic grou	1491913	1493055
Hypothetical, unclassified, unknown	1494959	1495492
Hypothetical, unclassified, unknown	1495635	1495997
Putative enzymes	1496920	1496087
Hypothetical, unclassified, unknown	1516433	1516687
Two-component regulatory systems	1518914	1519546
Hypothetical, unclassified, unknown	1519627	1519968
Hypothetical, unclassified, unknown	1526657	1526430
Carbon compound catabolism	1533238	1534278
Hypothetical, unclassified, unknown	1552641	1552997
Hypothetical, unclassified, unknown	1553112	1553675
Transcriptional regulators	1559122	1558880
Adaptation, protection	1559254	1559859
Hypothetical, unclassified, unknown	1572023	1572544
Motility & Attachment	1575290	1575559
Motility & Attachment	1583956	1584798
Two-component regulatory systems	1585640	1586014
Chemotaxis	1591286	1592176
Cell division	1592271	1593059
Chemotaxis	1594087	1594566
Hypothetical, unclassified, unknown	1594597	1595004
Hypothetical, unclassified, unknown	1596889	1597305
Hypothetical, unclassified, unknown	1599982	1599428

Transport of small molecules	1602179	1602880
Transport of small molecules	1602877	1603548
Transport of small molecules	1603671	1604429
Hypothetical, unclassified, unknown	1604426	1604602
Energy metabolism	1605088	1607061
Energy metabolism	1607065	1607607
Energy metabolism	1607604	1608071
Hypothetical, unclassified, unknown	1615908	1614670
Hypothetical, unclassified, unknown	1617085	1615895
Hypothetical, unclassified, unknown	1619907	1620263
Transport of small molecules	1624715	1623864
Transcriptional regulators	1634492	1633842
Hypothetical, unclassified, unknown	1638639	1638379
Hypothetical, unclassified, unknown	1639794	1638652
Hypothetical, unclassified, unknown	1647046	1646537
Hypothetical, unclassified, unknown	1649555	1648629
Hypothetical, unclassified, unknown	1649928	1650308
Transcriptional regulators	1660727	1661386
Cell division	1665065	1665934
DNA replication, recombination, modification	1666025	1668409
DNA replication, recombination, modification	1669989	1672034
Hypothetical, unclassified, unknown	1672080	1672406
Putative enzymes	1673204	1674352
Hypothetical, unclassified, unknown	1677559	1678407
Hypothetical, unclassified, unknown	1678590	1678261
Transport of small molecules	1678952	1678584
Hypothetical, unclassified, unknown	1684962	1684753
Energy metabolism	1689339	1687924
Energy metabolism	1694045	1693119
Hypothetical, unclassified, unknown	1696467	1697099
Hypothetical, unclassified, unknown	1697188	1697919
Hypothetical, unclassified, unknown	1697916	1698344
Hypothetical, unclassified, unknown	1704522	1704761
Hypothetical, unclassified, unknown	1709765	1709412
Hypothetical, unclassified, unknown	1712698	1712519
Energy metabolism	1720744	1721130
Energy metabolism	1721124	1721492
Energy metabolism	1721496	1723268
Energy metabolism	1723280	1723987
Energy metabolism	1728416	1729852
Energy metabolism	1730181	1731347
Energy metabolism	1731347	1732234
Hypothetical, unclassified, unknown	1734004	1734768
Hypothetical, unclassified, unknown	1735063	1734827
Hypothetical, unclassified, unknown	1735236	1735709
Hypothetical, unclassified, unknown	1735706	1736152
Hypothetical, unclassified, unknown	1736189	1737418
Fatty acid and phospholipid metabolism	1753418	1752903
Hypothetical, unclassified, unknown	1762433	1762870
Transcriptional regulators	1762928	1763752
Putative enzymes	1765345	1766205
Hypothetical, unclassified, unknown	1766285	1766947

Hypothetical, unclassified, unknown	1766956	1767762
Transcriptional regulators	1773682	1774548
Transport of small molecules	1775945	1776034
Transport of small molecules	1779877	1780428
Hypothetical, unclassified, unknown	1784108	1785016
Hypothetical, unclassified, unknown	1786888	1787166
Hypothetical, unclassified, unknown	1790879	1790472
Hypothetical, unclassified, unknown	1805218	1805724
Hypothetical, unclassified, unknown	1814995	1815135
Hypothetical, unclassified, unknown	1816352	1816858
Hypothetical, unclassified, unknown	1824969	1825430
Biosynthesis of cofactors, prosthetic grou	1826040	1825495
Hypothetical, unclassified, unknown	1826675	1826118
Hypothetical, unclassified, unknown	1827052	1826732
Amino acid biosynthesis and metabolism	1836367	1837227
Protein secretion/export apparatus	1841517	1840468
Protein secretion/export apparatus	1842302	1841514
Protein secretion/export apparatus	1845717	1845241
Protein secretion/export apparatus	1847227	1848093
Hypothetical, unclassified, unknown	1848707	1849072
Hypothetical, unclassified, unknown	1849077	1849406
Protein secretion/export apparatus	1851982	1852278
Protein secretion/export apparatus	1855862	1856299
Hypothetical, unclassified, unknown	1856308	1856553
Protein secretion/export apparatus	1862558	1862761
Protein secretion/export apparatus	1862764	1863021
Protein secretion/export apparatus	1863024	1863371
Protein secretion/export apparatus	1863799	1864137
Hypothetical, unclassified, unknown	1874967	1875767
Hypothetical, unclassified, unknown	1875849	1876580
Hypothetical, unclassified, unknown	1887297	1887058
Hypothetical, unclassified, unknown	1888186	1887698
Hypothetical, unclassified, unknown	1889173	1888985
Amino acid biosynthesis and metabolism	1891815	1890739
Amino acid biosynthesis and metabolism	1896630	1897247
Hypothetical, unclassified, unknown	1912756	1912217
Biosynthesis of cofactors, prosthetic grou	1917599	1918087
Transport of small molecules	1921174	1922226
Central intermediary metabolism	1926123	1925797
Transport of small molecules	1931775	1930564
Hypothetical, unclassified, unknown	1933632	1933054
Energy metabolism	1937644	1935035
Hypothetical, unclassified, unknown	1939583	1940206
Hypothetical, unclassified, unknown	1942442	1941720
Translation, post-translational modification	1943067	1944737
Translation, post-translational modification	1944747	1946129
Biosynthesis of cofactors, prosthetic grou	1947041	1946187
Translation, post-translational modification	1956227	1958623
DNA replication, recombination, modificat	1972959	1973405
Nucleotide biosynthesis and metabolism	1973470	1974210
Hypothetical, unclassified, unknown	1974627	1974238
Transport of small molecules	1979941	1978439

Hypothetical, unclassified, unknown	1984389	1985033
Hypothetical, unclassified, unknown	1989423	1989109
Hypothetical, unclassified, unknown	1993898	1993461
Hypothetical, unclassified, unknown	1995164	1994667
Hypothetical, unclassified, unknown	1998587	1998949
Hypothetical, unclassified, unknown	1999874	1999512
Hypothetical, unclassified, unknown	2004892	2004374
Hypothetical, unclassified, unknown	2007665	2008249
Hypothetical, unclassified, unknown	2012530	2012255
Hypothetical, unclassified, unknown	2015136	2014915
Transcriptional regulators	2019690	2018803
Transport of small molecules	2022398	2021712
Hypothetical, unclassified, unknown	2028454	2028981
Fatty acid and phospholipid metabolism	2031466	2031705
Hypothetical, unclassified, unknown	2034857	2034066
Transport of small molecules	2052941	2053264
Energy metabolism	2053277	2053675
Transcriptional regulators	2054223	2053672
Hypothetical, unclassified, unknown	2054309	2054842
Hypothetical, unclassified, unknown	2062401	2061664
Hypothetical, unclassified, unknown	2065545	2064853
Hypothetical, unclassified, unknown	2066767	2065493
Hypothetical, unclassified, unknown	2067955	2066786
Hypothetical, unclassified, unknown	2068728	2067961
Secreted Factors (toxins, enzymes, alginate)	2070685	2071173
Secreted Factors (toxins, enzymes, alginate)	2071209	2071697
Secreted Factors (toxins, enzymes, alginate)	2076311	2076958
Transcriptional regulators	2085426	2084476
Transcriptional regulators	2085929	2085423
Hypothetical, unclassified, unknown	2088034	2086808
Hypothetical, unclassified, unknown	2091837	2091490
Hypothetical, unclassified, unknown	2103294	2103770
Hypothetical, unclassified, unknown	2103770	2104096
Translation, post-translational modification	2109511	2108942
Hypothetical, unclassified, unknown	2109854	2109558
Hypothetical, unclassified, unknown	2117897	2118097
Hypothetical, unclassified, unknown	2118585	2118893
Hypothetical, unclassified, unknown	2118926	2119747
Hypothetical, unclassified, unknown	2122222	2120225
Hypothetical, unclassified, unknown	2137785	2136520
Hypothetical, unclassified, unknown	2138598	2137846
Hypothetical, unclassified, unknown	2141002	2140433
Hypothetical, unclassified, unknown	2141487	2140999
Hypothetical, unclassified, unknown	2145894	2146502
Hypothetical, unclassified, unknown	2146609	2146875
Hypothetical, unclassified, unknown	2148854	2149189
Hypothetical, unclassified, unknown	2150364	2149864
Hypothetical, unclassified, unknown	2150524	2150781
Hypothetical, unclassified, unknown	2157968	2159167
Transcriptional regulators	2164548	2163883
Two-component regulatory systems	2165876	2166553
Biosynthesis of cofactors, prosthetic groups	2171865	2171936

Biosynthesis of cofactors, prosthetic group	2171989	2172903
Biosynthesis of cofactors, prosthetic group	2173662	2173940
Hypothetical, unclassified, unknown	2181744	2181181
Hypothetical, unclassified, unknown	2182097	2181741
Chaperones & heat shock proteins	2182394	2182116
Fatty acid and phospholipid metabolism	2187065	2188246
Hypothetical, unclassified, unknown	2188459	2189883
Carbon compound catabolism	2196132	2195494
Transcriptional regulators	2198891	2199694
Putative enzymes	2203446	2202649
Fatty acid and phospholipid metabolism	2206353	2205190
Transcriptional regulators	2206806	2206402
Hypothetical, unclassified, unknown	2206999	2207928
Hypothetical, unclassified, unknown	2213539	2213315
Hypothetical, unclassified, unknown	2219099	2218098
Hypothetical, unclassified, unknown	2220275	2220574
Hypothetical, unclassified, unknown	2221157	2220903
Hypothetical, unclassified, unknown	2223804	2224478
Hypothetical, unclassified, unknown	2227541	2229001
Transport of small molecules	2234080	2235309
Transcriptional regulators	2244995	2245948
Central intermediary metabolism	2246456	2245986
Transport of small molecules	2256704	2257720
Putative enzymes	2259478	2260659
Hypothetical, unclassified, unknown	2265764	2265126
Translation, post-translational modification	2272460	2274568
Transport of small molecules	2277552	2278982
Hypothetical, unclassified, unknown	2278982	2279794
Hypothetical, unclassified, unknown	2281578	2279917
Hypothetical, unclassified, unknown	2290335	2289085
Hypothetical, unclassified, unknown	2297072	2297920
Hypothetical, unclassified, unknown	2300676	2301755
Transport of small molecules	2303022	2304215
Hypothetical, unclassified, unknown	2306627	2305782
Carbon compound catabolism	2307957	2309432
Hypothetical, unclassified, unknown	2312899	2313789
Biosynthesis of cofactors, prosthetic group	2314512	2315690
Putative enzymes	2316708	2317403
Hypothetical, unclassified, unknown	2318624	2318226
Hypothetical, unclassified, unknown	2322071	2321130
DNA replication, recombination, modification	2329348	2330424
Putative enzymes	2332059	2330959
Hypothetical, unclassified, unknown	2332820	2332392
Transcriptional regulators	2335172	2336104
Hypothetical, unclassified, unknown	2339987	2339352
Hypothetical, unclassified, unknown	2346477	2347838
Hypothetical, unclassified, unknown	2352430	2351906
Putative enzymes	2356713	2357573
Hypothetical, unclassified, unknown	2358024	2358311
Hypothetical, unclassified, unknown	2361706	2361873
Hypothetical, unclassified, unknown	2364816	2365058
Hypothetical, unclassified, unknown	2377476	2376538

Hypothetical, unclassified, unknown	2381778	2381473
Hypothetical, unclassified, unknown	2390255	2390620
Hypothetical, unclassified, unknown	2390949	2392046
Hypothetical, unclassified, unknown	2393424	2393633
Hypothetical, unclassified, unknown	2393708	2394178
Hypothetical, unclassified, unknown	2396252	2395944
Hypothetical, unclassified, unknown	2396883	2396536
Hypothetical, unclassified, unknown	2404655	2404386
Hypothetical, unclassified, unknown	2405233	2404949
Hypothetical, unclassified, unknown	2405739	2405230
Hypothetical, unclassified, unknown	2405993	2406877
Hypothetical, unclassified, unknown	2406961	2407131
Hypothetical, unclassified, unknown	2407236	2407661
Hypothetical, unclassified, unknown	2409837	2410181
Hypothetical, unclassified, unknown	2411709	2412122
Transcriptional regulators	2415661	2416245
Hypothetical, unclassified, unknown	2416376	2417413
Hypothetical, unclassified, unknown	2424400	2423924
Hypothetical, unclassified, unknown	2427017	2425497
Hypothetical, unclassified, unknown	2430170	2431129
Transport of small molecules	2433748	2435070
Transport of small molecules	2441555	2440347
Transcriptional regulators	2441771	2442691
Hypothetical, unclassified, unknown	2443161	2444366
Hypothetical, unclassified, unknown	2445533	2444886
Hypothetical, unclassified, unknown	2446564	2445545
Hypothetical, unclassified, unknown	2447325	2446597
Hypothetical, unclassified, unknown	2447989	2447573
Hypothetical, unclassified, unknown	2448533	2448033
Transcriptional regulators	2449545	2448568
Hypothetical, unclassified, unknown	2450765	2449554
Hypothetical, unclassified, unknown	2451707	2452426
Transport of small molecules	2457510	2458280
Hypothetical, unclassified, unknown	2468032	2469099
Hypothetical, unclassified, unknown	2472104	2472409
Hypothetical, unclassified, unknown	2479130	2478312
Amino acid biosynthesis and metabolism	2480844	2481830
Secreted Factors (toxins, enzymes, alginate)	2485471	2486118
Transcriptional regulators	2487293	2486355
Hypothetical, unclassified, unknown	2488950	2489732
Hypothetical, unclassified, unknown	2508775	2509467
Hypothetical, unclassified, unknown	2510622	2511050
Hypothetical, unclassified, unknown	2512511	2513182
Hypothetical, unclassified, unknown	2523239	2522958
Hypothetical, unclassified, unknown	2524201	2523236
Transport of small molecules	2525052	2524198
Transport of small molecules	2525846	2525049
Energy metabolism	2527657	2527412
Putative enzymes	2529467	2527743
Hypothetical, unclassified, unknown	2540082	2539063
Hypothetical, unclassified, unknown	2549748	2549906
Transcriptional regulators	2553965	2554858

Transport of small molecules	2571691	2570855
Hypothetical, unclassified, unknown	2573365	2572805
Hypothetical, unclassified, unknown	2579542	2580882
Transport of small molecules	2582097	2583407
Carbon compound catabolism	2587906	2589414
Hypothetical, unclassified, unknown	2593330	2594547
Hypothetical, unclassified, unknown	2595985	2596779
Transport of small molecules	2597869	2598522
Hypothetical, unclassified, unknown	2614893	2615438
Hypothetical, unclassified, unknown	2617019	2617516
Hypothetical, unclassified, unknown	2617529	2617954
Hypothetical, unclassified, unknown	2619695	2620711
Hypothetical, unclassified, unknown	2623284	2623856
Hypothetical, unclassified, unknown	2627175	2626780
Transcriptional regulators	2635971	2635051
Transport of small molecules	2645303	2646727
Hypothetical, unclassified, unknown	2689240	2689569
Hypothetical, unclassified, unknown	2689566	2690126
Putative enzymes	2694544	2693780
Hypothetical, unclassified, unknown	2694763	2694545
Hypothetical, unclassified, unknown	2701205	2702065
Hypothetical, unclassified, unknown	2705772	2706086
Hypothetical, unclassified, unknown	2723221	2722754
Hypothetical, unclassified, unknown	2724222	2723308
Hypothetical, unclassified, unknown	2724484	2724729
Hypothetical, unclassified, unknown	2730520	2729975
Hypothetical, unclassified, unknown	2732965	2732531
Hypothetical, unclassified, unknown	2738840	2739715
Amino acid biosynthesis and metabolism	2740882	2739761
Amino acid biosynthesis and metabolism	2747072	2746689
Hypothetical, unclassified, unknown	2753464	2752865
Hypothetical, unclassified, unknown	2754601	2754822
Hypothetical, unclassified, unknown	2755724	2756251
Hypothetical, unclassified, unknown	2756308	2756649
Hypothetical, unclassified, unknown	2760086	2759481
Hypothetical, unclassified, unknown	2760618	2760322
Hypothetical, unclassified, unknown	2761350	2760871
Hypothetical, unclassified, unknown	2781450	2780926
Transcriptional regulators	2786355	2785369
Transcriptional regulators	2787885	2786971
Central intermediary metabolism	2791219	2791863
Hypothetical, unclassified, unknown	2791905	2792816
Putative enzymes	2794132	2792798
Hypothetical, unclassified, unknown	2803344	2803622
Hypothetical, unclassified, unknown	2804131	2803859
Hypothetical, unclassified, unknown	2805916	2806290
Putative enzymes	2807368	2806349
Transcriptional regulators	2807468	2808511
Hypothetical, unclassified, unknown	2815281	2814766
Transport of small molecules	2817448	2818674
Hypothetical, unclassified, unknown	2818885	2818718
Hypothetical, unclassified, unknown	2822321	2821704

Carbon compound catabolism	2825590	2824658
Carbon compound catabolism	2833129	2832368
Carbon compound catabolism	2834689	2834201
Transport of small molecules	2841965	2840511
Fatty acid and phospholipid metabolism	2865104	2864169
Hypothetical, unclassified, unknown	2866199	2865747
Hypothetical, unclassified, unknown	2867505	2866192
Hypothetical, unclassified, unknown	2876409	2875696
Hypothetical, unclassified, unknown	2880519	2881562
Transcriptional regulators	2883156	2884088
Putative enzymes	2885332	2884205
Putative enzymes	2886551	2885361
Putative enzymes	2887336	2886569
Transcriptional regulators	2913921	2914358
Fatty acid and phospholipid metabolism	2923926	2923366
Transcriptional regulators	2934387	2933581
Hypothetical, unclassified, unknown	2945263	2945868
Hypothetical, unclassified, unknown	2948581	2948976
Hypothetical, unclassified, unknown	2948973	2949332
Hypothetical, unclassified, unknown	2949332	2949637
Hypothetical, unclassified, unknown	2949634	2949969
Translation, post-translational modification	2954695	2953415
Chaperones & heat shock proteins	2956778	2956152
Cell division	2959239	2956804
Translation, post-translational modification	2960455	2961135
Translation, post-translational modification	2962002	2962220
Hypothetical, unclassified, unknown	2964842	2964606
Transcription, RNA processing and degradation	2969986	2971113
Nucleotide biosynthesis and metabolism	2972698	2974068
Energy metabolism	2983204	2983881
Energy metabolism	2986242	2987588
Energy metabolism	2992001	2992501
Energy metabolism	2992547	2992855
Hypothetical, unclassified, unknown	3008323	3008009
Hypothetical, unclassified, unknown	3012536	3012279
Biosynthesis of cofactors, prosthetic groups	3015581	3015937
Hypothetical, unclassified, unknown	3016245	3016598
Hypothetical, unclassified, unknown	3016883	3016674
Protein secretion/export apparatus	3020928	3020503
Protein secretion/export apparatus	3021338	3020928
Protein secretion/export apparatus	3021741	3021307
Transport of small molecules	3025507	3024704
Transcriptional regulators	3028074	3029003
Amino acid biosynthesis and metabolism	3031397	3030435
Hypothetical, unclassified, unknown	3042501	3043415
Related to phage, transposon, or plasmid	3044765	3043749
Energy metabolism	3047969	3047643
Hypothetical, unclassified, unknown	3050611	3050330
Hypothetical, unclassified, unknown	3057375	3057608
Hypothetical, unclassified, unknown	3060659	3060264
Energy metabolism	3070365	3070703
Hypothetical, unclassified, unknown	3073731	3074417

Hypothetical, unclassified, unknown	3075217	3074579
Hypothetical, unclassified, unknown	3075410	3075889
Hypothetical, unclassified, unknown	3075921	3076313
Hypothetical, unclassified, unknown	3076343	3076621
Central intermediary metabolism	3079196	3079834
Hypothetical, unclassified, unknown	3089612	3088659
Hypothetical, unclassified, unknown	3090107	3089643
Hypothetical, unclassified, unknown	3094184	3093657
Hypothetical, unclassified, unknown	3096051	3094756
Hypothetical, unclassified, unknown	3098978	3098625
Hypothetical, unclassified, unknown	3099729	3099472
DNA replication, recombination, modification	3100111	3099809
Translation, post-translational modification	3102493	3100115
Translation, post-translational modification	3103544	3102528
Translation, post-translational modification	3103998	3103642
Translation, post-translational modification	3104216	3104022
Translation, post-translational modification	3104829	3104278
Translation, post-translational modification	3106751	3104829
DNA replication, recombination, modification	3110900	3111613
Hypothetical, unclassified, unknown	3114818	3115192
Hypothetical, unclassified, unknown	3117610	3117176
Hypothetical, unclassified, unknown	3119707	3119393
Hypothetical, unclassified, unknown	3122264	3121920
Hypothetical, unclassified, unknown	3122585	3122376
Putative enzymes	3126251	3127219
Hypothetical, unclassified, unknown	3127225	3127707
Hypothetical, unclassified, unknown	3128269	3127859
Hypothetical, unclassified, unknown	3132815	3132228
Hypothetical, unclassified, unknown	3133257	3132820
Hypothetical, unclassified, unknown	3137849	3138193
Hypothetical, unclassified, unknown	3138190	3138531
Hypothetical, unclassified, unknown	3139010	3139669
Hypothetical, unclassified, unknown	3141718	3142275
Hypothetical, unclassified, unknown	3142284	3142502
Hypothetical, unclassified, unknown	3142617	3143084
Hypothetical, unclassified, unknown	3149318	3148722
Hypothetical, unclassified, unknown	3152201	3150885
Hypothetical, unclassified, unknown	3155074	3154592
Hypothetical, unclassified, unknown	3156502	3156801
Hypothetical, unclassified, unknown	3157563	3156859
Hypothetical, unclassified, unknown	3158925	3159668
Hypothetical, unclassified, unknown	3160320	3160583
Hypothetical, unclassified, unknown	3162215	3161598
Hypothetical, unclassified, unknown	3162578	3162387
Transport of small molecules	3165541	3164762
Hypothetical, unclassified, unknown	3173174	3171597
Hypothetical, unclassified, unknown	3173243	3173722
Hypothetical, unclassified, unknown	3180951	3180553
Hypothetical, unclassified, unknown	3182399	3182851
Hypothetical, unclassified, unknown	3184001	3185128
Adaptation, protection	3185816	3185160
Hypothetical, unclassified, unknown	3192748	3193518

Putative enzymes	3197641	3198987
Hypothetical, unclassified, unknown	3200552	3200319
Translation, post-translational modification	3205079	3204513
Hypothetical, unclassified, unknown	3206252	3205122
Membrane proteins	3206914	3207165
Hypothetical, unclassified, unknown	3208260	3207289
Transcription, RNA processing and degradation	3212524	3213030
Secreted Factors (toxins, enzymes, alginate)	3215422	3216288
Hypothetical, unclassified, unknown	3221205	3221564
Hypothetical, unclassified, unknown	3228336	3227383
Nucleotide biosynthesis and metabolism	3230181	3229483
Transcriptional regulators	3231171	3230278
Transcriptional regulators	3232771	3231881
Hypothetical, unclassified, unknown	3235793	3235960
Hypothetical, unclassified, unknown	3249630	3249208
Hypothetical, unclassified, unknown	3253679	3253311
Hypothetical, unclassified, unknown	3255765	3255406
Hypothetical, unclassified, unknown	3265210	3264641
Hypothetical, unclassified, unknown	3271692	3270826
Hypothetical, unclassified, unknown	3272405	3271812
Putative enzymes	3277408	3278577
Hypothetical, unclassified, unknown	3284597	3283374
Hypothetical, unclassified, unknown	3291172	3290693
Hypothetical, unclassified, unknown	3291282	3291863
Hypothetical, unclassified, unknown	3291959	3292267
Putative enzymes	3297117	3295978
Putative enzymes	3308390	3309337
Energy metabolism	3311720	3310791
Energy metabolism	3312469	3311720
Energy metabolism	3312790	3314445
Motility & Attachment	3320029	3319673
DNA replication, recombination, modification	3321049	3320063
Nucleotide biosynthesis and metabolism	3321674	3321042
Hypothetical, unclassified, unknown	3322752	3321703
Fatty acid and phospholipid metabolism	3325182	3324946
Fatty acid and phospholipid metabolism	3326121	3325378
Fatty acid and phospholipid metabolism	3327082	3326144
Translation, post-translational modification	3328384	3328202
Hypothetical, unclassified, unknown	3328934	3328398
Transcription, RNA processing and degradation	3332303	3331347
Cell wall / LPS / capsule	3337230	3336211
Translation, post-translational modification	3337691	3337227
Cell wall / LPS / capsule	3338455	3337691
Hypothetical, unclassified, unknown	3338640	3338455
Cell wall / LPS / capsule	3339676	3338678
Hypothetical, unclassified, unknown	3340116	3339676
Transport of small molecules	3340748	3340113
Hypothetical, unclassified, unknown	3343177	3343710
Hypothetical, unclassified, unknown	3345099	3343798
Transport of small molecules	3345795	3345112
Hypothetical, unclassified, unknown	3347038	3345788
Hypothetical, unclassified, unknown	3346976	3347740

Nucleotide biosynthesis and metabolism	3350231	3348837
Hypothetical, unclassified, unknown	3350637	3350410
Energy metabolism	3354171	3353497
Putative enzymes	3360653	3359268
Nucleotide biosynthesis and metabolism	3365743	3365006
Hypothetical, unclassified, unknown	3369268	3369035
DNA replication, recombination, modification	3372705	3370099
Hypothetical, unclassified, unknown	3373170	3372796
Hypothetical, unclassified, unknown	3378511	3378948
Hypothetical, unclassified, unknown	3383947	3384333
Hypothetical, unclassified, unknown	3385183	3384377
Putative enzymes	3387828	3386269
Biosynthesis of cofactors, prosthetic groups	3394087	3394683
Hypothetical, unclassified, unknown	3397373	3397095
Hypothetical, unclassified, unknown	3398716	3399648
Hypothetical, unclassified, unknown	3403811	3404140
Hypothetical, unclassified, unknown	3404144	3404524
Hypothetical, unclassified, unknown	3404538	3404861
Hypothetical, unclassified, unknown	3409952	3409608
Translation, post-translational modification	3414400	3414612
Hypothetical, unclassified, unknown	3416066	3415785
Transcriptional regulators	3436429	3435986
Hypothetical, unclassified, unknown	3457909	3456542
Hypothetical, unclassified, unknown	3464151	3463888
Hypothetical, unclassified, unknown	3466959	3466072
Hypothetical, unclassified, unknown	3467084	3468049
Hypothetical, unclassified, unknown	3473017	3474135
Protein secretion/export apparatus	3476479	3475955
Protein secretion/export apparatus	3477629	3476481
Protein secretion/export apparatus	3480238	3479720
Protein secretion/export apparatus	3483421	3481913
Hypothetical, unclassified, unknown	3491410	3490751
Fatty acid and phospholipid metabolism	3493572	3492700
Amino acid biosynthesis and metabolism	3500597	3499485
Hypothetical, unclassified, unknown	3506241	3505864
Hypothetical, unclassified, unknown	3524489	3524160
Hypothetical, unclassified, unknown	3527733	3527428
Hypothetical, unclassified, unknown	3528349	3528230
Cell wall / LPS / capsule	3529446	3528427
Cell wall / LPS / capsule	3530457	3529507
Cell wall / LPS / capsule	3531707	3530466
Cell wall / LPS / capsule	3532814	3531750
Cell wall / LPS / capsule	3533932	3532811
Cell wall / LPS / capsule	3535080	3533947
Amino acid biosynthesis and metabolism	3535970	3535215
Amino acid biosynthesis and metabolism	3536578	3535970
Cell wall / LPS / capsule	3537810	3536575
Cell wall / LPS / capsule	3539123	3537807
Cell wall / LPS / capsule	3540206	3539127
Cell wall / LPS / capsule	3540784	3540209
Cell wall / LPS / capsule	3542670	3540781
Cell wall / LPS / capsule	3543689	3542739

Cell wall / LPS / capsule	3545073	3543763
Cell wall / LPS / capsule	3546926	3545880
DNA replication, recombination, modification	3547972	3547688
Translation, post-translational modification	3549788	3548109
Nucleotide biosynthesis and metabolism	3550745	3550056
Biosynthesis of cofactors, prosthetic groups	3556338	3555253
DNA replication, recombination, modification	3559197	3556426
Biosynthesis of cofactors, prosthetic groups	3562105	3562803
Hypothetical, unclassified, unknown	3569012	3568635
Carbon compound catabolism	3571602	3570940
Hypothetical, unclassified, unknown	3575696	3574845
Carbon compound catabolism	3587432	3588436
Hypothetical, unclassified, unknown	3593732	3594031
Hypothetical, unclassified, unknown	3594207	3594569
Hypothetical, unclassified, unknown	3597318	3597797
Transport of small molecules	3600453	3601598
Transcriptional regulators	3609075	3609839
Chaperones & heat shock proteins	3614303	3614866
Hypothetical, unclassified, unknown	3618466	3617342
Putative enzymes	3619618	3618992
Hypothetical, unclassified, unknown	3624836	3625057
Cell wall / LPS / capsule	3630604	3629666
Cell division	3632429	3632683
Transcription, RNA processing and degradation	3632787	3633422
Transcriptional regulators	3636256	3635540
Hypothetical, unclassified, unknown	3641232	3641810
Transcriptional regulators	3648065	3647754
Adaptation, protection	3653666	3653875
Hypothetical, unclassified, unknown	3668522	3667923
Hypothetical, unclassified, unknown	3668473	3668760
Hypothetical, unclassified, unknown	3669168	3668839
Hypothetical, unclassified, unknown	3671057	3670758
Transport of small molecules	3674323	3673007
Hypothetical, unclassified, unknown	3675159	3674569
Hypothetical, unclassified, unknown	3679945	3680460
Hypothetical, unclassified, unknown	3680967	3680464
Hypothetical, unclassified, unknown	3681047	3681460
Hypothetical, unclassified, unknown	3684716	3684162
Hypothetical, unclassified, unknown	3685761	3684904
Hypothetical, unclassified, unknown	3695480	3695178
Hypothetical, unclassified, unknown	3700315	3700785
Hypothetical, unclassified, unknown	3710224	3710679
Putative enzymes	3715804	3714914
Transport of small molecules	3716807	3717610
Transport of small molecules	3717604	3718437
Hypothetical, unclassified, unknown	3719328	3720056
Hypothetical, unclassified, unknown	3720122	3720622
Hypothetical, unclassified, unknown	3723444	3722989
Translation, post-translational modification	3730075	3729470
Putative enzymes	3740104	3741018
Hypothetical, unclassified, unknown	3742264	3742689
Fatty acid and phospholipid metabolism	3743699	3743938

Hypothetical, unclassified, unknown	3747455	3747165
Transcriptional regulators	3752477	3752043
Hypothetical, unclassified, unknown	3759680	3759375
Chemotaxis	3760819	3759995
Hypothetical, unclassified, unknown	3762803	3763126
Hypothetical, unclassified, unknown	3763680	3764471
Hypothetical, unclassified, unknown	3765086	3764475
Secreted Factors (toxins, enzymes, alginate)	3772560	3771502
Hypothetical, unclassified, unknown	3778265	3778603
Putative enzymes	3778703	3779368
Hypothetical, unclassified, unknown	3779929	3780075
Hypothetical, unclassified, unknown	3780127	3780312
Hypothetical, unclassified, unknown	3787478	3787020
Transport of small molecules	3790985	3790149
Hypothetical, unclassified, unknown	3794116	3793814
Energy metabolism	3801103	3801930
Energy metabolism	3801947	3802483
Energy metabolism	3803342	3802566
Hypothetical, unclassified, unknown	3808802	3808317
Transport of small molecules	3814574	3813957
Hypothetical, unclassified, unknown	3820005	3820271
Hypothetical, unclassified, unknown	3820307	3820891
Energy metabolism	3823515	3822514
Hypothetical, unclassified, unknown	3840747	3840358
Transcriptional regulators	3840843	3841736
Related to phage, transposon, or plasmid	3843289	3842273
Hypothetical, unclassified, unknown	3844104	3843652
Biosynthesis of cofactors, prosthetic group	3845774	3846334
Biosynthesis of cofactors, prosthetic group	3846336	3846707
Transport of small molecules	3849582	3848794
Hypothetical, unclassified, unknown	3850751	3849603
Hypothetical, unclassified, unknown	3851800	3850829
Hypothetical, unclassified, unknown	3852512	3851919
Adaptation, protection	3856130	3855492
Hypothetical, unclassified, unknown	3856336	3856545
Putative enzymes	3867706	3869463
Hypothetical, unclassified, unknown	3882979	3883437
Hypothetical, unclassified, unknown	3885710	3886306
Transcriptional regulators	3890649	3889924
Translation, post-translational modification	3895323	3897356
Hypothetical, unclassified, unknown	3906390	3907088
Hypothetical, unclassified, unknown	3907267	3907851
Hypothetical, unclassified, unknown	3910738	3911772
Hypothetical, unclassified, unknown	3912409	3913131
DNA replication, recombination, modification	3913128	3913766
Hypothetical, unclassified, unknown	3913875	3914054
Hypothetical, unclassified, unknown	3918468	3918250
Hypothetical, unclassified, unknown	3918787	3918470
Hypothetical, unclassified, unknown	3922072	3921269
Transport of small molecules	3928333	3927557
Hypothetical, unclassified, unknown	3936836	3935799
Hypothetical, unclassified, unknown	3937431	3937237

Transport of small molecules	3943806	3942649
Transcription, RNA processing and degradation	3948137	3948811
Hypothetical, unclassified, unknown	3949852	3950073
Hypothetical, unclassified, unknown	3952386	3952060
Secreted Factors (toxins, enzymes, alginate)	3965841	3967010
Secreted Factors (toxins, enzymes, alginate)	3977183	3977833
Hypothetical, unclassified, unknown	3986879	3987292
Hypothetical, unclassified, unknown	3997821	3998114
Carbon compound catabolism	4003600	4002107
Hypothetical, unclassified, unknown	4004782	4004958
Hypothetical, unclassified, unknown	4007506	4008036
Hypothetical, unclassified, unknown	4010326	4009541
Carbon compound catabolism	4023176	4021971
Hypothetical, unclassified, unknown	4035757	4035605
Hypothetical, unclassified, unknown	4036020	4035757
Hypothetical, unclassified, unknown	4039173	4040099
Hypothetical, unclassified, unknown	4040819	4040103
Transport of small molecules	4043060	4043830
Hypothetical, unclassified, unknown	4045159	4045569
Hypothetical, unclassified, unknown	4045588	4045809
Hypothetical, unclassified, unknown	4051557	4051096
DNA replication, recombination, modification	4052603	4051563
Hypothetical, unclassified, unknown	4062898	4062425
Hypothetical, unclassified, unknown	4067294	4067542
Hypothetical, unclassified, unknown	4068307	4067603
Hypothetical, unclassified, unknown	4068611	4068327
Carbon compound catabolism	4069965	4068676
Cell wall / LPS / capsule	4070856	4070011
Nucleotide biosynthesis and metabolism	4072487	4070859
Hypothetical, unclassified, unknown	4073986	4072658
Fatty acid and phospholipid metabolism	4075006	4074056
DNA replication, recombination, modification	4078677	4075156
Cell wall / LPS / capsule	4082180	4081044
Cell wall / LPS / capsule	4082960	4082184
Fatty acid and phospholipid metabolism	4083397	4082957
Cell wall / LPS / capsule	4084504	4083443
Transport of small molecules	4085010	4084504
Transport of small molecules	4087454	4085061
Biosynthesis of cofactors, prosthetic groups	4090093	4088903
Fatty acid and phospholipid metabolism	4090905	4090090
Cell wall / LPS / capsule	4091654	4090899
Translation, post-translational modification	4092227	4091670
Nucleotide biosynthesis and metabolism	4092967	4092230
Translation, post-translational modification	4094035	4093166
Translation, post-translational modification	4094906	4094166
Translation, post-translational modification	4095171	4095956
Hypothetical, unclassified, unknown	4102767	4103060
Hypothetical, unclassified, unknown	4103731	4104078
Cell wall / LPS / capsule	4104744	4105778
Transport of small molecules	4111080	4110346
Hypothetical, unclassified, unknown	4114932	4115330
Transcriptional regulators	4120468	4121106

Hypothetical, unclassified, unknown	4123955	4123260
Hypothetical, unclassified, unknown	4126089	4125742
Hypothetical, unclassified, unknown	4126843	4126163
Hypothetical, unclassified, unknown	4130598	4130942
Hypothetical, unclassified, unknown	4135972	4135451
Translation, post-translational modification	4143664	4142569
Chemotaxis	4148251	4145942
Hypothetical, unclassified, unknown	4165879	4165718
DNA replication, recombination, modification	4172484	4170769
Hypothetical, unclassified, unknown	4173067	4172528
Hypothetical, unclassified, unknown	4182018	4181377
Hypothetical, unclassified, unknown	4182769	4182074
Hypothetical, unclassified, unknown	4183709	4184938
Translation, post-translational modification	4195357	4195007
Transcription, RNA processing and degradation	4196157	4195399
Transcription, RNA processing and degradation	4196691	4196164
Translation, post-translational modification	4196958	4196707
Protein secretion/export apparatus	4198541	4197168
Hypothetical, unclassified, unknown	4204736	4204542
Hypothetical, unclassified, unknown	4205906	4205295
Hypothetical, unclassified, unknown	4206664	4207164
Putative enzymes	4209255	4210277
Hypothetical, unclassified, unknown	4221796	4221212
Hypothetical, unclassified, unknown	4224115	4223567
Nucleotide biosynthesis and metabolism	4227236	4225659
Hypothetical, unclassified, unknown	4231070	4232227
Transcriptional regulators	4234274	4235182
DNA replication, recombination, modification	4235219	4236598
Transcriptional regulators	4242294	4241341
Hypothetical, unclassified, unknown	4243651	4243079
Hypothetical, unclassified, unknown	4244184	4243708
Hypothetical, unclassified, unknown	4244875	4245723
Hypothetical, unclassified, unknown	4245809	4246204
Hypothetical, unclassified, unknown	4255323	4254736
Hypothetical, unclassified, unknown	4260396	4259254
Hypothetical, unclassified, unknown	4263492	4262377
Motility & Attachment	4265287	4264529
Hypothetical, unclassified, unknown	4266444	4265305
Nucleotide biosynthesis and metabolism	4266900	4266469
Hypothetical, unclassified, unknown	4267344	4267144
Energy metabolism	4267709	4267371
Chaperones & heat shock proteins	4269575	4267716
Chaperones & heat shock proteins	4270139	4269618
Biosynthesis of cofactors, prosthetic groups	4270470	4270147
Biosynthesis of cofactors, prosthetic groups	4270884	4270498
Hypothetical, unclassified, unknown	4272655	4272164
Protein secretion/export apparatus	4278946	4277084
Hypothetical, unclassified, unknown	4279344	4279006
Hypothetical, unclassified, unknown	4285483	4284416
Hypothetical, unclassified, unknown	4286594	4285476
Hypothetical, unclassified, unknown	4287709	4286786
Hypothetical, unclassified, unknown	4290866	4291234

Translation, post-translational modification	4291355	4294207
Hypothetical, unclassified, unknown	4294604	4294254
Hypothetical, unclassified, unknown	4302040	4303050
Hypothetical, unclassified, unknown	4305063	4305425
Hypothetical, unclassified, unknown	4311861	4310950
Hypothetical, unclassified, unknown	4312702	4311950
Hypothetical, unclassified, unknown	4314794	4314480
Hypothetical, unclassified, unknown	4316037	4315555
Hypothetical, unclassified, unknown	4316824	4316108
Putative enzymes	4318258	4318905
DNA replication, recombination, modification	4330320	4330895
Hypothetical, unclassified, unknown	4331451	4332461
Hypothetical, unclassified, unknown	4332652	4333035
Transport of small molecules	4343527	4342121
Hypothetical, unclassified, unknown	4350352	4350738
Hypothetical, unclassified, unknown	4351594	4352493
Transport of small molecules	4354543	4355265
Transport of small molecules	4356200	4356862
Transport of small molecules	4356875	4358038
Hypothetical, unclassified, unknown	4359074	4358166
Hypothetical, unclassified, unknown	4373937	4374332
Hypothetical, unclassified, unknown	4374329	4374856
Hypothetical, unclassified, unknown	4374849	4375232
Hypothetical, unclassified, unknown	4382015	4381500
Biosynthesis of cofactors, prosthetic groups	4386351	4385899
Biosynthesis of cofactors, prosthetic groups	4386607	4386356
Biosynthesis of cofactors, prosthetic groups	4387086	4386604
Transport of small molecules	4414949	4414131
DNA replication, recombination, modification	4418302	4418583
Hypothetical, unclassified, unknown	4439376	4439783
Hypothetical, unclassified, unknown	4442452	4442868
Transcriptional regulators	4444977	4445486
Hypothetical, unclassified, unknown	4445998	4446390
Hypothetical, unclassified, unknown	4447132	4448217
Transcriptional regulators	4453182	4452535
Biosynthesis of cofactors, prosthetic groups	4457361	4458644
Hypothetical, unclassified, unknown	4459749	4459417
Hypothetical, unclassified, unknown	4461387	4462409
Hypothetical, unclassified, unknown	4462399	4462881
Translation, post-translational modification	4463903	4465438
Hypothetical, unclassified, unknown	4466753	4466322
Translation, post-translational modification	4466924	4469545
Hypothetical, unclassified, unknown	4469612	4470235
DNA replication, recombination, modification	4470273	4471310
Hypothetical, unclassified, unknown	4471402	4471554
Related to phage, transposon, or plasmid	4473622	4474638
Biosynthesis of cofactors, prosthetic groups	4477976	4476993
Hypothetical, unclassified, unknown	4478907	4478626
Cell wall / LPS / capsule	4483363	4482260
Hypothetical, unclassified, unknown	4486179	4485823
Hypothetical, unclassified, unknown	4486846	4486202
Putative enzymes	4488409	4489632

Secreted Factors (toxins, enzymes, algina	4713795	4714283
Secreted Factors (toxins, enzymes, algina	4714313	4714801
Secreted Factors (toxins, enzymes, algina	4714825	4716042
Secreted Factors (toxins, enzymes, algina	4718556	4719392
Secreted Factors (toxins, enzymes, algina	4719418	4720062
Hypothetical, unclassified, unknown	4724034	4722850
Transport of small molecules	4744818	4745123
DNA replication, recombination, modificat	4747136	4746639
Translation, post-translational modification	4754378	4753989
Transcription, RNA processing and degra	4755423	4754422
Translation, post-translational modification	4756066	4755446
Translation, post-translational modification	4756472	4756083
Translation, post-translational modification	4756847	4756491
Translation, post-translational modification	4757094	4756978
Protein secretion/export apparatus	4758451	4757123
Translation, post-translational modification	4758886	4758452
Translation, post-translational modification	4759066	4758890
Translation, post-translational modification	4759569	4759069
Translation, post-translational modification	4759923	4759573
Translation, post-translational modification	4760467	4759934
Translation, post-translational modification	4760871	4760479
Translation, post-translational modification	4761366	4761061
Translation, post-translational modification	4761919	4761380
Translation, post-translational modification	4762253	4761939
Translation, post-translational modification	4762634	4762266
Translation, post-translational modification	4762924	4762658
Translation, post-translational modification	4763118	4762927
Translation, post-translational modification	4763531	4763118
Translation, post-translational modification	4764229	4763543
Translation, post-translational modification	4764574	4764242
Translation, post-translational modification	4764862	4764587
Translation, post-translational modification	4765700	4764879
Translation, post-translational modification	4766011	4765712
Translation, post-translational modification	4766610	4766008
Translation, post-translational modification	4767259	4766624
Translation, post-translational modification	4767653	4767342
Translation, post-translational modification	4771655	4771185
Translation, post-translational modification	4772126	4771755
Transcription, RNA processing and degra	4776477	4772278
Transcription, RNA processing and degra	4780616	4776543
Translation, post-translational modification	4781206	4780838
Translation, post-translational modification	4781785	4781285
Translation, post-translational modification	4782679	4781984
Translation, post-translational modification	4783110	4782679
Transcription, RNA processing and degra	4783760	4783227
Protein secretion/export apparatus	4784138	4783770
Hypothetical, unclassified, unknown	4787479	4786733
Hypothetical, unclassified, unknown	4819927	4820409
Two-component regulatory systems	4820531	4821358
Hypothetical, unclassified, unknown	4823363	4823079
Hypothetical, unclassified, unknown	4824123	4823386
Hypothetical, unclassified, unknown	4830553	4829642

Hypothetical, unclassified, unknown	4830963	4831181
Nucleotide biosynthesis and metabolism	4843551	4842700
Hypothetical, unclassified, unknown	4851309	4852316
Hypothetical, unclassified, unknown	4854008	4853649
Carbon compound catabolism	4856959	4858410
Putative enzymes	4859262	4858489
Transcriptional regulators	4870327	4869557
Hypothetical, unclassified, unknown	4875244	4874654
Hypothetical, unclassified, unknown	4877605	4876820
Hypothetical, unclassified, unknown	4878586	4877690
Hypothetical, unclassified, unknown	4878789	4879544
Hypothetical, unclassified, unknown	4882052	4882354
Hypothetical, unclassified, unknown	4884960	4884718
Hypothetical, unclassified, unknown	4887505	4887278
Adaptation, protection	4893696	4894277
Hypothetical, unclassified, unknown	4902201	4903295
Hypothetical, unclassified, unknown	4909403	4909161
Hypothetical, unclassified, unknown	4914509	4914126
Chaperones & heat shock proteins	4917123	4915480
Chaperones & heat shock proteins	4917467	4917174
Hypothetical, unclassified, unknown	4918932	4918198
Putative enzymes	4919041	4919799
Hypothetical, unclassified, unknown	4921980	4922363
Hypothetical, unclassified, unknown	4925794	4925315
Protein secretion/export apparatus	4936615	4933865
Hypothetical, unclassified, unknown	4937819	4938214
Cell wall / LPS / capsule	4939186	4938275
Cell division	4940483	4939299
Cell division	4941787	4940534
Cell division	4942672	4941809
Cell wall / LPS / capsule	4945074	4943632
Cell wall / LPS / capsule	4946140	4945067
Cell division	4947329	4946130
Cell wall / LPS / capsule	4948675	4947329
Cell wall / LPS / capsule	4949771	4948689
Cell wall / LPS / capsule	4951147	4949771
Cell wall / LPS / capsule	4952603	4951140
Cell wall / LPS / capsule	4954342	4952603
Cell division	4954632	4954339
Hypothetical, unclassified, unknown	4955570	4954629
Hypothetical, unclassified, unknown	4956028	4955573
Hypothetical, unclassified, unknown	4959519	4959896
Putative enzymes	4959925	4960518
Adaptation, protection	4961557	4961150
Adaptation, protection	4962186	4961569
Energy metabolism	4964265	4963054
Translation, post-translational modification	4965500	4965108
Translation, post-translational modification	4965943	4965515
Transcriptional regulators	4968711	4969610
Hypothetical, unclassified, unknown	4971890	4970796
Translation, post-translational modification	4973331	4971985
Hypothetical, unclassified, unknown	4974028	4973399

Cell wall / LPS / capsule	4985469	4984204
Hypothetical, unclassified, unknown	4986154	4985846
Hypothetical, unclassified, unknown	4986798	4986151
Hypothetical, unclassified, unknown	4987283	4986810
Transport of small molecules	4988081	4987284
Hypothetical, unclassified, unknown	4989304	4990284
Hypothetical, unclassified, unknown	4990832	4991404
Hypothetical, unclassified, unknown	4991391	4991918
Transport of small molecules	4991918	4992643
Transcriptional regulators	4992869	4994362
Hypothetical, unclassified, unknown	4994440	4994748
Transport of small molecules	4994762	4995226
Transport of small molecules	4996118	4996390
Hypothetical, unclassified, unknown	5000303	4999908
Cell division	5012313	5011321
Cell division	5013430	5012393
Translation, post-translational modification	5013670	5013960
Translation, post-translational modification	5013973	5015427
Translation, post-translational modification	5015534	5016979
Hypothetical, unclassified, unknown	5017039	5017416
Hypothetical, unclassified, unknown	5028230	5027421
Transcriptional regulators	5036244	5036807
Hypothetical, unclassified, unknown	5046663	5046031
Biosynthesis of cofactors, prosthetic group	5068031	5068879
Motility & Attachment	5069530	5069081
Motility & Attachment	5069762	5071462
Motility & Attachment	5071566	5072690
Hypothetical, unclassified, unknown	5073563	5074174
Hypothetical, unclassified, unknown	5074171	5074371
Hypothetical, unclassified, unknown	5077535	5077705
Transcription, RNA processing and degradation	5091814	5090852
Two-component regulatory systems	5094984	5096321
Motility & Attachment	5099262	5100086
Motility & Attachment	5100083	5100670
Adaptation, protection	5105929	5104985
Translation, post-translational modification	5106957	5106448
Translation, post-translational modification	5109781	5106950
Biosynthesis of cofactors, prosthetic group	5110743	5109805
Translation, post-translational modification	5112662	5112937
Hypothetical, unclassified, unknown	5113468	5113004
Amino acid biosynthesis and metabolism	5114598	5113480
Adaptation, protection	5115889	5114669
Translation, post-translational modification	5116288	5116031
Translation, post-translational modification	5116623	5116312
Biosynthesis of cofactors, prosthetic group	5116864	5117832
Hypothetical, unclassified, unknown	5122386	5121898
Hypothetical, unclassified, unknown	5122901	5122560
Hypothetical, unclassified, unknown	5125930	5125604
Hypothetical, unclassified, unknown	5135815	5136192
Transcriptional regulators	5155560	5156123
Hypothetical, unclassified, unknown	5162448	5162068
Hypothetical, unclassified, unknown	5168754	5169188

Hypothetical, unclassified, unknown	5169504	5169250
Hypothetical, unclassified, unknown	5174979	5176103
Hypothetical, unclassified, unknown	5197880	5198323
Hypothetical, unclassified, unknown	5204927	5206087
Hypothetical, unclassified, unknown	5206486	5206208
Hypothetical, unclassified, unknown	5207006	5206719
Hypothetical, unclassified, unknown	5210995	5210705
Hypothetical, unclassified, unknown	5212104	5211631
Nucleotide biosynthesis and metabolism	5212832	5213470
Hypothetical, unclassified, unknown	5215669	5216202
Chaperones & heat shock proteins	5216763	5217551
Biosynthesis of cofactors, prosthetic grou	5223561	5222539
Cell wall / LPS / capsule	5230910	5230113
Biosynthesis of cofactors, prosthetic grou	5231658	5230900
Translation, post-translational modification	5233566	5232484
Translation, post-translational modification	5234852	5233584
Cell wall / LPS / capsule	5236773	5237390
Biosynthesis of cofactors, prosthetic grou	5237392	5238240
Nucleotide biosynthesis and metabolism	5238407	5239348
Translation, post-translational modification	5239465	5240079
Translation, post-translational modification	5240121	5240705
Hypothetical, unclassified, unknown	5242558	5242253
Putative enzymes	5246122	5245475
Hypothetical, unclassified, unknown	5248771	5248070
Hypothetical, unclassified, unknown	5250617	5249598
Fatty acid and phospholipid metabolism	5272299	5271484
Amino acid biosynthesis and metabolism	5275731	5274007
Hypothetical, unclassified, unknown	5276282	5276734
Hypothetical, unclassified, unknown	5277171	5276842
Hypothetical, unclassified, unknown	5277950	5277171
Hypothetical, unclassified, unknown	5282158	5282505
Transport of small molecules	5286034	5285267
Hypothetical, unclassified, unknown	5291613	5291960
Hypothetical, unclassified, unknown	5297482	5297006
Biosynthesis of cofactors, prosthetic grou	5310725	5311213
Biosynthesis of cofactors, prosthetic grou	5311463	5312263
Biosynthesis of cofactors, prosthetic grou	5313205	5313585
Energy metabolism	5313675	5315339
Hypothetical, unclassified, unknown	5322234	5322449
Hypothetical, unclassified, unknown	5322706	5322509
Hypothetical, unclassified, unknown	5323100	5322756
Transcription, RNA processing and degra	5325478	5323373
Translation, post-translational modification	5325921	5325652
Translation, post-translational modification	5329948	5327426
Transcription, RNA processing and degra	5331457	5329976
Hypothetical, unclassified, unknown	5331960	5331502
Protein secretion/export apparatus	5332742	5332353
Energy metabolism	5333500	5332745
Cell wall / LPS / capsule	5334903	5333566
Biosynthesis of cofactors, prosthetic grou	5335771	5334920
Cell division	5338522	5337899
Hypothetical, unclassified, unknown	5338617	5338931

Hypothetical, unclassified, unknown	5343754	5343104
Amino acid biosynthesis and metabolism	5345891	5345085
Chaperones & heat shock proteins	5349760	5349200
Transcriptional regulators	5352078	5351674
Transport of small molecules	5352176	5352706
Hypothetical, unclassified, unknown	5353506	5353072
Hypothetical, unclassified, unknown	5361585	5362067
Two-component regulatory systems	5364070	5364735
Transcriptional regulators	5366256	5366654
Hypothetical, unclassified, unknown	5370720	5370475
Hypothetical, unclassified, unknown	5376851	5377708
Hypothetical, unclassified, unknown	5377790	5378095
Hypothetical, unclassified, unknown	5378092	5378841
Hypothetical, unclassified, unknown	5380447	5379512
Related to phage, transposon, or plasmid	5383811	5382795
Hypothetical, unclassified, unknown	5386999	5387721
Energy metabolism	5396858	5395929
Fatty acid and phospholipid metabolism	5402944	5402015
Hypothetical, unclassified, unknown	5414487	5414278
Hypothetical, unclassified, unknown	5418568	5418350
Hypothetical, unclassified, unknown	5419862	5420317
Transcriptional regulators	5422505	5423065
Hypothetical, unclassified, unknown	5434651	5434115
Fatty acid and phospholipid metabolism	5442303	5442773
Fatty acid and phospholipid metabolism	5442791	5444140
Translation, post-translational modification	5445198	5446082
Transcription, RNA processing and degradation	5448642	5448965
Transport of small molecules	5460525	5461382
Central intermediary metabolism	5462762	5463604
Hypothetical, unclassified, unknown	5463917	5464435
Central intermediary metabolism	5464820	5466520
Hypothetical, unclassified, unknown	5468282	5468016
Hypothetical, unclassified, unknown	5468408	5469022
Hypothetical, unclassified, unknown	5472041	5471625
Hypothetical, unclassified, unknown	5472438	5472734
Transcriptional regulators	5473765	5474577
Two-component regulatory systems	5480401	5481090
Transport of small molecules	5483767	5482451
Hypothetical, unclassified, unknown	5486355	5486984
Biosynthesis of cofactors, prosthetic groups	5487714	5488385
Hypothetical, unclassified, unknown	5489040	5489612
Transcriptional regulators	5490651	5489629
Transcriptional regulators	5505783	5505070
Hypothetical, unclassified, unknown	5507897	5506965
Hypothetical, unclassified, unknown	5517093	5516398
Biosynthesis of cofactors, prosthetic groups	5519710	5520537
Hypothetical, unclassified, unknown	5522385	5522972
Hypothetical, unclassified, unknown	5524718	5523867
Hypothetical, unclassified, unknown	5525904	5524969
DNA replication, recombination, modification	5535555	5534161
Translation, post-translational modification	5537288	5537058
Translation, post-translational modification	5537737	5537318

Nucleotide biosynthesis and metabolism	5543364	5542072
Hypothetical, unclassified, unknown	5544820	5544635
Hypothetical, unclassified, unknown	5548644	5548396
Translation, post-translational modification	5549721	5548750
Hypothetical, unclassified, unknown	5553583	5553116
Hypothetical, unclassified, unknown	5556934	5557953
Central intermediary metabolism	5561598	5562413
Hypothetical, unclassified, unknown	5569089	5570627
Hypothetical, unclassified, unknown	5570624	5571160
DNA replication, recombination, modification	5574485	5572221
Hypothetical, unclassified, unknown	5575017	5574493
Hypothetical, unclassified, unknown	5576027	5575014
DNA replication, recombination, modification	5577916	5576027
Hypothetical, unclassified, unknown	5579498	5578680
Hypothetical, unclassified, unknown	5580961	5581707
Putative enzymes	5593423	5592632
Cell wall / LPS / capsule	5605097	5603820
Antibiotic resistance and susceptibility	5606102	5606434
Hypothetical, unclassified, unknown	5606495	5607670
Hypothetical, unclassified, unknown	5607667	5608479
Transport of small molecules	5615543	5613732
Hypothetical, unclassified, unknown	5615651	5616301
Hypothetical, unclassified, unknown	5626378	5624900
Hypothetical, unclassified, unknown	5627133	5626375
Hypothetical, unclassified, unknown	5627864	5627130
Cell wall / LPS / capsule	5628670	5627864
Cell wall / LPS / capsule	5629788	5628667
Cell wall / LPS / capsule	5630852	5629785
Cell wall / LPS / capsule	5631886	5630849
Hypothetical, unclassified, unknown	5659184	5658417
Transcriptional regulators	5662741	5663814
Hypothetical, unclassified, unknown	5663888	5664868
Biosynthesis of cofactors, prosthetic group	5666056	5664989
Amino acid biosynthesis and metabolism	5675701	5675183
Motility & Attachment	5680712	5679648
DNA replication, recombination, modification	5687495	5689714
Translation, post-translational modification	5689963	5691726
Hypothetical, unclassified, unknown	5691761	5692456
Hypothetical, unclassified, unknown	5702113	5701697
Biosynthesis of cofactors, prosthetic group	5702668	5703438
Hypothetical, unclassified, unknown	5703453	5704079
Hypothetical, unclassified, unknown	5704076	5705677
Amino acid biosynthesis and metabolism	5706190	5706525
Protein secretion/export apparatus	5706551	5706799
Hypothetical, unclassified, unknown	5708035	5708742
Chemotaxis	5708954	5710897
Hypothetical, unclassified, unknown	5720468	5720944
Transcriptional regulators	5723581	5724537
Carbon compound catabolism	5753473	5752463
Central intermediary metabolism	5754143	5753613
Transcriptional regulators	5762149	5762574
Amino acid biosynthesis and metabolism	5766483	5767892

Protein secretion/export apparatus	5777096	5776605
Nucleotide biosynthesis and metabolism	5777387	5777133
Hypothetical, unclassified, unknown	5777808	5777389
Carbon compound catabolism	5778133	5779680
Hypothetical, unclassified, unknown	5779994	5780812
Amino acid biosynthesis and metabolism	5791085	5790444
Hypothetical, unclassified, unknown	5791836	5792234
Hypothetical, unclassified, unknown	5797064	5797336
Transport of small molecules	5802128	5802823
Cell wall / LPS / capsule	5810280	5811338
Cell wall / LPS / capsule	5811335	5812243
Cell wall / LPS / capsule	5812240	5813121
Cell wall / LPS / capsule	5813121	5813666
Amino acid biosynthesis and metabolism	5824786	5825718
Hypothetical, unclassified, unknown	5829469	5828903
Hypothetical, unclassified, unknown	5830749	5830312
Hypothetical, unclassified, unknown	5835481	5835894
Putative enzymes	5840894	5839104
Putative enzymes	5843799	5843197
Chaperones & heat shock proteins	5848366	5847971
Putative enzymes	5879970	5878753
Hypothetical, unclassified, unknown	5880481	5879999
Translation, post-translational modification	5883012	5881678
Hypothetical, unclassified, unknown	5883576	5883022
Hypothetical, unclassified, unknown	5883971	5884285
Hypothetical, unclassified, unknown	5885485	5885943
Hypothetical, unclassified, unknown	5896726	5895260
Transcription, RNA processing and degradation	5900123	5898864
Energy metabolism	5900694	5900368
Hypothetical, unclassified, unknown	5907389	5907862
Hypothetical, unclassified, unknown	5908329	5907847
Biosynthesis of cofactors, prosthetic groups	5921496	5920741
Biosynthesis of cofactors, prosthetic groups	5922434	5921493
Hypothetical, unclassified, unknown	5941081	5940746
Cell wall / LPS / capsule	5941335	5941475
Amino acid biosynthesis and metabolism	5942744	5943574
Putative enzymes	5945234	5945932
Central intermediary metabolism	5952820	5952482
DNA replication, recombination, modification	5962715	5964724
Energy metabolism	5969764	5969354
Hypothetical, unclassified, unknown	5972202	5971849
Translation, post-translational modification	5986118	5985882
DNA replication, recombination, modification	5989319	5988645
DNA replication, recombination, modification	5989459	5990667
Nucleotide biosynthesis and metabolism	5990675	5991130
Hypothetical, unclassified, unknown	5996035	5996985
Energy metabolism	6000142	5999753
Hypothetical, unclassified, unknown	6001377	6000760
Nucleotide biosynthesis and metabolism	6002039	6001398
Hypothetical, unclassified, unknown	6003329	6002958
Transcription, RNA processing and degradation	6004095	6003376
Hypothetical, unclassified, unknown	6004276	6005139

Nucleotide biosynthesis and metabolism	6005198	6005809
Hypothetical, unclassified, unknown	6008397	6008777
Hypothetical, unclassified, unknown	6017013	6016621
Carbon compound catabolism	6018996	6018829
Carbon compound catabolism	6019347	6019180
Biosynthesis of cofactors, prosthetic group	6025304	6026194
Two-component regulatory systems	6032267	6031365
Hypothetical, unclassified, unknown	6060199	6059822
Hypothetical, unclassified, unknown	6063831	6063352
Putative enzymes	6069098	6067944
Hypothetical, unclassified, unknown	6074229	6075206
Transcriptional regulators	6082866	6083072
Hypothetical, unclassified, unknown	6083104	6083508
Hypothetical, unclassified, unknown	6083752	6084084
Hypothetical, unclassified, unknown	6084544	6084368
Carbon compound catabolism	6096706	6097026
Hypothetical, unclassified, unknown	6148318	6149181
Hypothetical, unclassified, unknown	6151313	6151525
Hypothetical, unclassified, unknown	6155202	6154783
Hypothetical, unclassified, unknown	6158178	6158942
Translation, post-translational modification	6159562	6158948
Hypothetical, unclassified, unknown	6171732	6171926
Hypothetical, unclassified, unknown	6172872	6172711
Hypothetical, unclassified, unknown	6188854	6188165
Transport of small molecules	6195308	6196315
Hypothetical, unclassified, unknown	6219068	6218856
Transport of small molecules	6221100	6222857
Transport of small molecules	6225924	6224896
Hypothetical, unclassified, unknown	6227081	6227449
Hypothetical, unclassified, unknown	6228243	6227602
Hypothetical, unclassified, unknown	6236228	6235830
Central intermediary metabolism	6244945	6243110
Cell wall / LPS / capsule	6247689	6246325
Energy metabolism	6248235	6247810
Energy metabolism	6249653	6248277
Energy metabolism	6250544	6249684
Energy metabolism	6252139	6250595
Energy metabolism	6252694	6252158
Energy metabolism	6253176	6252706
Energy metabolism	6253491	6253234
Energy metabolism	6254410	6253541
Energy metabolism	6254807	6254427
Cell division	6255843	6254971
Hypothetical, unclassified, unknown	6260053	6259670
Hypothetical, unclassified, unknown	6263563	6261827
Translation, post-translational modification	6264211	6263804
Translation, post-translational modification	6264360	6264226

Pat ID	Int length	Prob	Gene Name
4269	4200	0.9999719	rpoC
4270	4074	0.9999719	rpoB
3640	3522	0.9999058	dnaE
1156	2892	0.9995054	nrdA
3834	2853	0.9994519	valS
4560	2832	0.9994208	ileS
595	2775	0.999327	ostA
3168	2772	0.9993217	gyrA
4403	2751	0.9992831	secA
903	2625	0.9990012	alaS
3987	2622	0.9989933	leuS
1787	2610	0.998961	acnB
3011	2607	0.9989528	topA
4744	2523	0.9986937	infB
2615	2436	0.9983575	ftsK
4	2421	0.9982914	gyrB
1803	2397	0.99818	lon
3648	2394	0.9981655	
1529	2385	0.9981216	lig
2739	2379	0.9980917	pheT
3704	2310	0.9977116	
4964	2265	0.9974239	parC
5050	2220	0.9971	priA
260	2151	0.9965225	
1372	2136	0.9963824	
2071	2109	0.996116	fusA2
4740	2106	0.9960852	pnp
8	2055	0.9955228	glyS
1532	2046	0.9954155	dnaX
3482	2034	0.9952684	metG
5296	2010	0.9949599	rep
1939	1998	0.9947981	
1480	1974	0.9944589	ccmF
5072	1944	0.9940037	
2744	1923	0.9936629	thrS
1068	1911	0.9934596	
1596	1905	0.9933555	htpG
3157	1890	0.9930879	
4967	1890	0.9930879	parE
4044	1884	0.9929779	dxs
1370	1866	0.9926372	
3821	1863	0.9925788	secD
3810	1860	0.99252	hscA
1810	1848	0.99228	
5549	1836	0.9920322	glmS
4997	1812	0.9915127	msbA
767	1800	0.9912404	lepA
5187	1791	0.9910304	
1583	1773	0.9905952	sdhA
5051	1764	0.9903698	argS
5529	1758	0.9902165	

3460	1758	0.9902165	
4418	1740	0.9897418	ftsI
5568	1737	0.9896605	
2298	1725	0.9893287	
4696	1725	0.9893287	ilvI
3725	1716	0.9890729	recJ
956	1716	0.9890729	proS
4868	1701	0.9886329	ureC
4526	1701	0.9886329	pilB
3162	1680	0.9879869	rpsA
1794	1671	0.987699	glnS
4732	1665	0.9875032	pgi
2075	1662	0.9874041	
2953	1656	0.9872036	
4385	1644	0.986793	groEL
3637	1629	0.9862612	pyrG
1251	1626	0.9861522	
183	1611	0.9855946	atsA
5065	1602	0.9852493	
3769	1578	0.9842875	guaA
2818	1578	0.9842875	
3024	1560	0.9835251	
5131	1548	0.9829965	pgm
1331	1548	0.9829965	
1	1545	0.9828617	dnaA
5556	1545	0.9828617	atpA
4961	1539	0.9825889	
3984	1536	0.9824509	int
2207	1521	0.9817442	
2343	1509	0.9811584	mtlY
3103	1509	0.9811584	xcpR
1820	1503	0.9808585	nhaB
985	1497	0.9805538	
3570	1494	0.9803997	mmsA
4462	1494	0.9803997	rpoN
443	1491	0.9802443	
4745	1482	0.9797707	nusA
5006	1479	0.9796104	
2097	1476	0.9794487	
5237	1467	0.9789561	
4417	1464	0.9787893	murE
2037	1461	0.9786211	
202	1458	0.9784516	
427	1458	0.9784516	oprM
2521	1455	0.9782808	czcB
4483	1455	0.9782808	gatA
4329	1452	0.9781087	pykA
913	1449	0.9779351	mgtE
4484	1446	0.9777602	gatB
4411	1443	0.9775839	murC
1587	1437	0.9772271	lpdG
2073	1431	0.9768646	

2002	1425	0.9764964	
2391	1425	0.9764964	
1551	1416	0.975933	
5119	1410	0.9755499	glnA
686	1410	0.9755499	
3876	1407	0.9753561	narK2
704	1395	0.9745653	
2991	1395	0.9745653	sth
4931	1395	0.9745653	dnaB
3001	1386	0.9739556	
1795	1383	0.9737491	cysS
3777	1380	0.973541	xseA
4416	1377	0.9733313	murF
5554	1377	0.9733313	atpD
3746	1374	0.9731199	ffh
2629	1371	0.9729068	purB
373	1368	0.972692	ftsY
1217	1368	0.972692	
3081	1368	0.972692	
2131	1362	0.9722573	
2729	1350	0.9713671	
119	1350	0.9713671	
4848	1350	0.9713671	accC
4439	1347	0.9711402	trpS
4414	1347	0.9711402	murD
2641	1347	0.9711402	nuoF
2843	1347	0.9711402	
2336	1341	0.9706808	
4547	1338	0.9704484	pilR
4749	1338	0.9704484	glmM
5224	1335	0.9702141	pepP
2475	1335	0.9702141	
3638	1329	0.96974	
4243	1329	0.96974	secY
716	1326	0.9695001	
2214	1323	0.9692583	
2794	1317	0.968769	
4887	1317	0.968769	
3280	1317	0.968769	oprO
3154	1317	0.968769	wzy
2539	1314	0.9685214	
3159	1311	0.9682719	wbpA
2338	1311	0.9682719	
1183	1311	0.9682719	dctA
1120	1308	0.9680204	
4099	1305	0.9677669	
2986	1302	0.9675113	
972	1299	0.9672538	tolB
2734	1296	0.9669942	
4938	1293	0.9667326	purA
594	1293	0.9667326	surA
3635	1290	0.9664688	eno

1215	1287	0.966203	
3977	1284	0.9659351	hemL
2612	1281	0.9656651	serS
4988	1278	0.9653929	waaA
1895	1275	0.9651185	
1373	1269	0.9645633	fabF2
4666	1269	0.9645633	hemA
4450	1266	0.9642824	murA
1951	1266	0.9642824	
5239	1260	0.9637139	rho
4408	1254	0.9631363	ftsA
2080	1251	0.9628441	
2988	1251	0.9628441	
1155	1248	0.9625495	nrdB
3147	1242	0.9619534	wbpJ
1488	1239	0.9616518	
904	1239	0.9616518	lysC
3153	1236	0.9613478	wzx
3733	1230	0.9607326	
1595	1230	0.9607326	
2042	1230	0.9607326	
1914	1227	0.9604213	
2500	1227	0.9604213	
446	1224	0.9601075	
4008	1224	0.9601075	
2928	1224	0.9601075	
4566	1221	0.9597913	obg
5221	1218	0.9594726	
2347	1218	0.9594726	
4212	1218	0.9594726	
687	1215	0.9591513	
273	1215	0.9591513	
1352	1212	0.9588275	
1783	1212	0.9588275	nasA
4430	1212	0.9588275	
2228	1212	0.9588275	
5320	1209	0.9585011	dfp
2219	1209	0.9585011	opdE
1098	1209	0.9585011	fleS
3589	1206	0.9581721	
501	1206	0.9581721	bioF
2221	1206	0.9581721	
4413	1200	0.9575063	ftsW
1974	1200	0.9575063	
4190	1197	0.9571695	
1107	1197	0.9571695	
2092	1194	0.9568299	
2553	1191	0.9564877	
1489	1191	0.9564877	
3650	1191	0.9564877	dxr
546	1191	0.9564877	metK
4407	1185	0.9557951	ftsZ

4219	1185	0.9557951	
2062	1182	0.9554447	
2001	1182	0.9554447	atoB
2103	1179	0.9550915	
559	1179	0.9550915	
4991	1176	0.9547355	
3542	1170	0.954015	
1896	1170	0.954015	
2922	1170	0.954015	
1588	1167	0.9536505	sucC
787	1164	0.953283	
3891	1164	0.953283	
2015	1164	0.953283	
552	1164	0.953283	pgk
4636	1161	0.9529127	
3773	1158	0.9525394	
3523	1158	0.9525394	
5390	1155	0.9521632	
1237	1152	0.951784	
1162	1152	0.951784	dapE
3444	1149	0.9514018	
1535	1149	0.9514018	
3096	1149	0.9514018	xcpY
3211	1146	0.9510165	
1375	1143	0.9506282	pdxB
3800	1143	0.9506282	
1509	1143	0.9506282	
2940	1140	0.9502368	
3806	1140	0.9502368	
3643	1137	0.9498423	lpxB
3150	1134	0.9494447	wbpG
2852	1131	0.949044	
2626	1128	0.94864	trmU
2552	1128	0.94864	
2831	1128	0.94864	
4617	1125	0.9482329	
4527	1125	0.9482329	pilC
105	1125	0.9482329	coxB
3230	1125	0.9482329	
4056	1122	0.9478225	ribD
3149	1122	0.9478225	wbpH
2442	1122	0.9478225	gcvT2
2509	1122	0.9478225	catB
5010	1122	0.9478225	waaG
574	1122	0.9478225	
4565	1119	0.9474089	proB
3828	1119	0.9474089	
3093	1119	0.9474089	
3803	1116	0.946992	
689	1113	0.9465718	
3117	1113	0.9465718	asd
4002	1104	0.9452911	rodA

2119	1101	0.9448574	
146	1098	0.9444202	
2167	1098	0.9444202	
3701	1096	0.9441269	prfB
4373	1095	0.9439796	
4438	1095	0.9439796	
643	1092	0.9435355	
3969	1086	0.9426368	
3167	1086	0.9426368	serC
4665	1083	0.9421821	prfA
4415	1083	0.9421821	mraY
2090	1080	0.9417237	
3155	1080	0.9417237	wbpE
1750	1077	0.9412617	
2118	1077	0.9412617	ada
5032	1074	0.9407961	
4412	1074	0.9407961	murG
5034	1068	0.9398537	hemE
2242	1068	0.9398537	
5011	1068	0.9398537	waaC
3827	1068	0.9398537	
555	1065	0.9393769	fda
5044	1065	0.9393769	pilM
3148	1065	0.9393769	wbpl
945	1062	0.9388964	purM
3646	1062	0.9388964	lpxD
1004	1059	0.938412	nadA
3360	1059	0.938412	
4097	1059	0.938412	
69	1059	0.938412	
5161	1059	0.938412	rmlB
1777	1053	0.9374317	oprF
646	1053	0.9374317	
2963	1050	0.9369357	
1690	1050	0.9369357	pseU
3160	1047	0.9364357	wzz
971	1044	0.9359319	tolA
2492	1044	0.9359319	mexT
2549	1044	0.9359319	
1409	1041	0.935424	aphA
4149	1041	0.935424	
3617	1041	0.935424	recA
5012	1038	0.9349121	waaF
3519	1038	0.9349121	
2197	1038	0.9349121	
4481	1038	0.9349121	mreB
98	1038	0.9349121	
3989	1038	0.9349121	holA
3666	1035	0.9343961	dapD
203	1035	0.9343961	
82	1035	0.9343961	
3492	1035	0.9343961	

5531	1029	0.9333519	tonB
580	1026	0.9328235	gcp
4655	1023	0.932291	hemH
3981	1023	0.932291	
3759	1023	0.932291	
4895	1023	0.932291	
2977	1020	0.9317542	murB
4681	1020	0.9317542	
4151	1020	0.9317542	acoB
4952	1020	0.9317542	
2491	1020	0.9317542	
2303	1020	0.9317542	
3145	1020	0.9317542	wbpL
2223	1020	0.9317542	
3434	1017	0.9312132	
1102	1017	0.9312132	fliG
2370	1017	0.9312132	
4797	1017	0.9312132	
2690	1017	0.9312132	
3993	1017	0.9312132	
445	1017	0.9312132	
2740	1017	0.9312132	pheS
2060	1017	0.9312132	
4966	1014	0.930668	
3868	1011	0.9301183	
5110	1011	0.9301183	fbp
3840	1011	0.9301183	
5503	1008	0.9295644	
4322	1008	0.9295644	
498	1008	0.9295644	
4209	1005	0.929006	
402	1005	0.929006	pyrB
3195	1005	0.929006	gapA
2026	1002	0.9284432	
4238	1002	0.9284432	rpoA
3416	1002	0.9284432	
2981	999	0.927876	lpxK
4480	993	0.9267279	mreC
927	990	0.9261471	ldhA
280	990	0.9261471	cysA
143	990	0.9261471	
593	987	0.9255616	pdxA
2467	987	0.9255616	
2961	987	0.9255616	holB
2253	987	0.9255616	ansA
26	987	0.9255616	
728	984	0.9249716	
3996	984	0.9249716	lipA
5033	981	0.9243768	
4457	981	0.9243768	
5396	978	0.9237773	
2227	978	0.9237773	

3445	972	0.922564	
2854	972	0.922564	
4945	972	0.922564	miaA
4569	969	0.9219502	ispB
660	969	0.9219502	
543	969	0.9219502	
2767	969	0.9219502	
4051	969	0.9219502	thiL
3089	966	0.9213315	
2293	966	0.9213315	
851	963	0.9207078	
2683	963	0.9207078	
4544	963	0.9207078	rluD
2211	960	0.9200793	
1213	960	0.9200793	
2975	957	0.9194457	rluC
5085	957	0.9194457	
715	957	0.9194457	
2051	954	0.9188071	
2874	954	0.9188071	
815	954	0.9188071	
3782	954	0.9188071	
407	954	0.9188071	gshB
2730	954	0.9188071	
2407	954	0.9188071	
3639	951	0.9181635	accA
479	951	0.9181635	
3146	951	0.9181635	wbpK
3158	951	0.9181635	wbpB
1911	951	0.9181635	
5325	951	0.9181635	
9	948	0.9175148	glyQ
2949	948	0.9175148	
4557	945	0.9168609	lytB
759	945	0.9168609	
829	942	0.9162018	
4670	942	0.9162018	prs
2110	942	0.9162018	
4420	942	0.9162018	
5260	942	0.9162018	hemC
233	942	0.9162018	
3242	939	0.9155375	
2258	939	0.9155375	ptxR
159	939	0.9155375	
2157	939	0.9155375	
2968	939	0.9155375	fabD
4561	939	0.9155375	ribF
4926	936	0.914868	
4792	936	0.914868	
2536	936	0.914868	
3036	933	0.9141931	
5173	933	0.9141931	arcC

4170	933	0.9141931	
2551	933	0.9141931	
2507	933	0.9141931	catA
869	933	0.9141931	pbpG
2123	933	0.9141931	
4908	933	0.9141931	
4068	930	0.9135129	
4813	930	0.9135129	lipC
2681	930	0.9135129	
2951	930	0.9135129	etfA
4809	930	0.9135129	fdhE
2017	930	0.9135129	
3605	927	0.9128273	
1517	927	0.9128273	
4037	927	0.9128273	
1555	927	0.9128273	
477	927	0.9128273	
3829	924	0.9121363	
4174	924	0.9121363	
205	921	0.9114397	
100	921	0.9114397	
2220	921	0.9114397	
2383	921	0.9114397	
133	918	0.9107377	
771	918	0.9107377	era
2469	915	0.9100301	
1986	915	0.9100301	pqqB
113	915	0.9100301	
2689	915	0.9100301	
70	915	0.9100301	
3330	915	0.9100301	
2428	915	0.9100301	
3850	912	0.9093169	
2474	912	0.9093169	
4305	912	0.9093169	
4406	912	0.9093169	lpxC
3776	909	0.908598	
448	909	0.908598	
1638	909	0.908598	
1342	909	0.908598	
5162	909	0.908598	rmlD
3892	909	0.908598	
1328	909	0.908598	
702	906	0.9078734	
1000	906	0.9078734	
1145	903	0.9071431	
730	903	0.9071431	
5364	903	0.9071431	
4436	900	0.906407	
3886	900	0.906407	
932	900	0.906407	cysM
705	900	0.906407	

4349	897	0.9056651	
1223	894	0.9049173	
2316	894	0.9049173	
2877	894	0.9049173	
207	894	0.9049173	
3433	894	0.9049173	
1321	891	0.9041635	cyoE
3312	891	0.9041635	
2879	891	0.9041635	
5358	891	0.9041635	ubiA
1461	891	0.9041635	
2101	891	0.9041635	
11	888	0.9034038	
1859	888	0.9034038	
1589	888	0.9034038	sucD
3088	888	0.9034038	
4043	888	0.9034038	ispA
2185	885	0.9026381	
4850	885	0.9026381	prmA
5163	882	0.9018663	rmlA
209	882	0.9018663	
188	882	0.9018663	
1010	879	0.9010883	dapA
2830	876	0.9003042	htpX
412	876	0.9003042	pilK
1138	876	0.9003042	
1135	876	0.9003042	
2441	876	0.9003042	
5562	873	0.8995139	spoOJ
626	873	0.8995139	
3112	873	0.8995139	accD
3655	870	0.8987173	tsf
1528	870	0.8987173	zipA
5560	870	0.8987173	atpB
1698	867	0.8979144	popN
2863	867	0.8979144	lipH
2915	867	0.8979144	
1630	867	0.8979144	
5335	864	0.8971052	
5457	864	0.8971052	
4409	864	0.8971052	ftsQ
211	864	0.8971052	mdcD
5555	861	0.8962895	atpG
1622	861	0.8962895	
2418	861	0.8962895	
2142	861	0.8962895	
1687	861	0.8962895	speE
4861	858	0.8954674	
4788	858	0.8954674	
3292	858	0.8954674	
2294	855	0.8946387	
244	855	0.8946387	

708	855	0.8946387	
1796	855	0.8946387	folD
376	855	0.8946387	rpoH
768	855	0.8946387	lepB
3185	852	0.8938035	
4314	852	0.8938035	purU1
4750	852	0.8938035	folP
4925	852	0.8938035	
1496	852	0.8938035	
4669	849	0.8929616	ipk
1539	849	0.8929616	
2088	849	0.8929616	
4524	849	0.8929616	nadC
3787	849	0.8929616	
2095	846	0.8921131	
3636	846	0.8921131	kdsA
1364	843	0.8912579	
4864	843	0.8912579	ureD
1454	843	0.8912579	
184	840	0.8903958	
4215	837	0.889527	
3384	837	0.889527	phnC
2329	837	0.889527	
3315	834	0.8886512	
1379	834	0.8886512	
5278	831	0.8877685	dapF
4296	828	0.8868789	
978	828	0.8868789	
4920	828	0.8868789	nadE
3395	828	0.8868789	nosY
503	825	0.8859821	
1619	825	0.8859821	
4552	825	0.8859821	pilW
3348	825	0.8859821	
1938	822	0.8850783	
4260	822	0.8850783	rplB
2251	819	0.8841673	
4167	819	0.8841673	
3936	819	0.8841673	
4969	819	0.8841673	
5132	819	0.8841673	
238	816	0.883249	
3651	816	0.883249	cdsA
4693	816	0.883249	pssA
187	816	0.883249	
4956	816	0.883249	rhdA
790	816	0.883249	
1164	813	0.8823235	
820	813	0.8823235	
2074	813	0.8823235	
4992	813	0.8823235	
4878	813	0.8823235	

204	810	0.8813907	
4492	810	0.8813907	
2591	807	0.8804504	
1624	807	0.8804504	
4759	807	0.8804504	dapB
3022	807	0.8804504	
5009	807	0.8804504	waaP
35	807	0.8804504	trpA
3314	804	0.8795027	
3505	804	0.8795027	
2678	804	0.8795027	
2010	804	0.8795027	
1732	801	0.8785475	
341	801	0.8785475	lgt
4729	801	0.8785475	panB
4662	798	0.8775847	murl
550	798	0.8775847	
4455	798	0.8775847	
2295	798	0.8775847	
2013	798	0.8775847	
416	795	0.8766143	
2349	795	0.8766143	
342	795	0.8766143	thyA
1872	792	0.8756362	
3353	792	0.8756362	
4980	792	0.8756362	
1691	789	0.8746503	pscT
642	789	0.8746503	
4651	789	0.8746503	
4157	789	0.8746503	
1462	789	0.8746503	
3443	789	0.8746503	
3578	786	0.8736566	
3657	786	0.8736566	map
4348	786	0.8736566	
2260	783	0.8726551	
862	783	0.8726551	
236	780	0.8716456	
2811	780	0.8716456	
1224	780	0.8716456	
4122	780	0.8716456	
4699	780	0.8716456	
3644	777	0.8706281	lpxA
3397	777	0.8706281	fpr
3512	777	0.8706281	
1307	774	0.8696025	
4330	774	0.8696025	
3609	771	0.8685688	potC
5063	771	0.8685688	ubiE
1366	771	0.8685688	
611	771	0.8685688	priR
639	771	0.8685688	

4341	771	0.8685688	
2839	771	0.8685688	
2234	771	0.8685688	
4706	768	0.8675269	
1897	768	0.8675269	
2554	768	0.8675269	
5028	768	0.8675269	
2979	765	0.8664768	kdsB
216	765	0.8664768	
5469	765	0.8664768	
3220	765	0.8664768	
2411	765	0.8664768	
1591	765	0.8664768	
2989	765	0.8664768	
1088	762	0.8654183	
2515	762	0.8654183	xylL
1021	762	0.8654183	
4663	759	0.8643515	moeB
4389	759	0.8643515	
1012	759	0.8643515	
1477	759	0.8643515	ccmC
5007	759	0.8643515	
3743	759	0.8643515	trmD
3805	759	0.8643515	pilF
3151	756	0.8632761	hisF2
4350	756	0.8632761	
4748	756	0.8632761	tpiA
5259	756	0.8632761	hemD
3652	756	0.8632761	uppS
339	756	0.8632761	
1125	753	0.8621923	
3851	753	0.8621923	
1369	753	0.8621923	
1952	753	0.8621923	
182	753	0.8621923	
309	753	0.8621923	
2952	750	0.8610999	etfB
4790	750	0.8610999	
1350	750	0.8610999	
4049	747	0.8599988	
1216	747	0.8599988	
4972	747	0.8599988	
4279	747	0.8599988	
2967	744	0.8588889	fabG
2803	744	0.8588889	
544	744	0.8588889	
4083	741	0.8577703	
1816	741	0.8577703	dnaQ
3656	741	0.8577703	rpsB
4299	738	0.8566428	
1892	738	0.8566428	
3004	738	0.8566428	

3654	738	0.8566428	pyrH
4388	735	0.8555064	
3671	735	0.8555064	
5008	735	0.8555064	
1559	732	0.854361	
1733	732	0.854361	
1165	729	0.8532064	
2224	729	0.8532064	
3317	729	0.8532064	
3477	726	0.8520428	rhIR
489	726	0.8520428	
4461	726	0.8520428	
1792	723	0.8508699	
3494	723	0.8508699	
4802	723	0.8508699	
502	723	0.8508699	
3888	723	0.8508699	
4181	720	0.8496877	
2229	720	0.8496877	
5334	720	0.8496877	rph
531	717	0.8484961	
3857	717	0.8484961	
3249	717	0.8484961	
3606	717	0.8484961	
906	714	0.8472951	
2749	714	0.8472951	endA
4906	714	0.8472951	
2544	714	0.8472951	
1106	714	0.8472951	
993	714	0.8472951	
1157	711	0.8460846	
1013	711	0.8460846	purC
1584	708	0.8448644	sdhB
1348	708	0.8448644	
5071	708	0.8448644	
58	705	0.8436346	
947	705	0.8436346	
3633	705	0.8436346	
2800	705	0.8436346	
4064	705	0.8436346	
1475	702	0.8423951	ccmA
1371	702	0.8423951	
4679	702	0.8423951	
279	699	0.8411457	
3171	699	0.8411457	ubiG
5281	699	0.8411457	
2876	699	0.8411457	pyrF
3488	699	0.8411457	
3681	696	0.8398864	
4273	696	0.8398864	rplA
3731	696	0.8398864	
5154	696	0.8398864	

4916	696	0.8398864	
2105	696	0.8398864	
5052	696	0.8398864	
969	696	0.8398864	tolQ
1894	693	0.8386172	
2280	693	0.8386172	
213	693	0.8386172	
733	693	0.8386172	
3163	690	0.8373379	cmk
5496	690	0.8373379	
4885	690	0.8373379	irlR
4257	687	0.8360484	rpsC
2719	687	0.8360484	
120	687	0.8360484	
504	687	0.8360484	bioD
1862	687	0.8360484	modB
527	684	0.8347487	dnr
1118	684	0.8347487	
2987	684	0.8347487	
2617	681	0.8334387	aat
3685	681	0.8334387	
2638	678	0.8321183	nuoB
1980	678	0.8321183	
2034	675	0.8307875	
1261	675	0.8307875	
2996	675	0.8307875	nqrD
3528	675	0.8307875	mnt
453	675	0.8307875	
976	675	0.8307875	
5319	675	0.8307875	radC
607	675	0.8307875	rpe
2284	672	0.8294461	
1167	672	0.8294461	
1476	672	0.8294461	ccmB
1193	672	0.8294461	
4892	672	0.8294461	ureF
330	672	0.8294461	rpiA
944	669	0.8280941	purN
1269	669	0.8280941	
243	669	0.8280941	
167	666	0.8267314	
65	666	0.8267314	
4029	666	0.8267314	
3368	666	0.8267314	
1978	666	0.8267314	
4776	666	0.8267314	
1623	663	0.8253578	
3181	663	0.8253578	
3890	663	0.8253578	
1090	663	0.8253578	
697	663	0.8253578	
1526	660	0.8239734	

2782	660	0.8239734	
3110	660	0.8239734	
4055	660	0.8239734	ribC
4121	660	0.8239734	
2832	657	0.822578	tpm
2351	654	0.8211715	
3550	651	0.8197539	algF
4998	651	0.8197539	
4757	651	0.8197539	
1504	651	0.8197539	
1049	648	0.818325	pdxH
655	648	0.818325	
2222	648	0.818325	
3859	648	0.818325	
2257	648	0.818325	pvcD
3973	648	0.818325	
4676	648	0.818325	
4453	648	0.818325	
1905	648	0.818325	
4216	645	0.8168848	
4006	645	0.8168848	
2473	645	0.8168848	
1825	645	0.8168848	
652	645	0.8168848	vfr
251	642	0.8154332	
5331	642	0.8154332	pyrE
5142	642	0.8154332	hisH1
5534	642	0.8154332	
3730	642	0.8154332	
2007	639	0.8139701	maiA
2726	639	0.8139701	
2720	639	0.8139701	
4646	639	0.8139701	upp
826	639	0.8139701	
3495	639	0.8139701	nth
3678	639	0.8139701	
3450	639	0.8139701	
2066	639	0.8139701	
990	639	0.8139701	
4182	639	0.8139701	
2983	636	0.8124954	
3246	636	0.8124954	rluA
114	636	0.8124954	
4263	636	0.8124954	rplC
2126	636	0.8124954	
4507	633	0.811009	
1558	633	0.811009	
1397	633	0.811009	
2962	633	0.811009	tmk
4890	630	0.8095108	
629	630	0.8095108	
4019	630	0.8095108	

4440	630	0.8095108	
3232	627	0.8080008	
2614	627	0.8080008	lolA
5064	627	0.8080008	
853	624	0.8064788	
3665	624	0.8064788	
1790	624	0.8064788	
4752	624	0.8064788	ftsJ
981	624	0.8064788	
3988	624	0.8064788	
5341	621	0.8049447	
4239	621	0.8049447	rpsD
1757	618	0.8033984	thrH
2504	618	0.8033984	
4668	618	0.8033984	
4428	618	0.8033984	sspA
5330	618	0.8033984	
4047	618	0.8033984	ribA
2807	618	0.8033984	
3407	618	0.8033984	hasAp
1315	615	0.8018399	
5470	615	0.8018399	
4671	615	0.8018399	
1219	615	0.8018399	
571	615	0.8018399	
4871	615	0.8018399	
3754	612	0.800269	
3354	612	0.800269	
4529	612	0.800269	
5336	612	0.800269	gmk
3152	609	0.7986857	hisH2
1962	609	0.7986857	
2459	606	0.7970898	
154	606	0.7970898	pcaG
2602	606	0.7970898	
1432	606	0.7970898	lasI
3326	606	0.7970898	
377	606	0.7970898	
4262	603	0.7954813	rplD
1089	603	0.7954813	
5190	603	0.7954813	
3273	600	0.7938601	
2451	600	0.7938601	
3472	597	0.7922259	
370	597	0.7922259	
3030	597	0.7922259	
2792	597	0.7922259	
1172	597	0.7922259	napC
3446	594	0.7905789	
4012	594	0.7905789	
2916	594	0.7905789	
4425	594	0.7905789	

684	594	0.7905789	
4345	591	0.7889187	
4063	591	0.7889187	
3281	591	0.7889187	
3796	588	0.7872454	
2774	588	0.7872454	
4553	588	0.7872454	pilX
4923	588	0.7872454	
763	585	0.7855589	mucA
2196	585	0.7855589	
3765	585	0.7855589	
1847	585	0.7855589	
3489	585	0.7855589	
3414	585	0.7855589	
4672	585	0.7855589	
1280	585	0.7855589	
4366	582	0.7838589	sodB
2936	582	0.7838589	
3255	579	0.7821455	
1785	579	0.7821455	
111	579	0.7821455	
358	579	0.7821455	
3867	576	0.7804185	
3156	576	0.7804185	wbpD
776	573	0.7786779	
3784	573	0.7786779	
4894	573	0.7786779	
4459	573	0.7786779	
2372	573	0.7786779	
2910	570	0.7769234	
1928	570	0.7769234	rimJ
475	570	0.7769234	
1955	570	0.7769234	
422	570	0.7769234	
405	570	0.7769234	
2851	567	0.775155	efp
5176	567	0.775155	
1994	564	0.7733726	
4600	564	0.7733726	nfxB
4499	564	0.7733726	
4171	564	0.7733726	
139	564	0.7733726	ahpC
3227	564	0.7733726	ppiA
1427	564	0.7733726	
2331	561	0.7715761	
2406	561	0.7715761	
3438	561	0.7715761	folE1
4831	561	0.7715761	
4762	561	0.7715761	grpE
2584	561	0.7715761	pgsA
1204	558	0.7697653	
1675	558	0.7697653	

3653	558	0.7697653	frr
22	558	0.7697653	
2784	558	0.7697653	
3291	555	0.7679402	
5225	555	0.7679402	
535	555	0.7679402	
1472	555	0.7679402	
311	555	0.7679402	
2743	552	0.7661006	infC
1635	552	0.7661006	kdpC
1884	552	0.7661006	
54	549	0.7642464	
3767	549	0.7642464	
1543	549	0.7642464	apt
2365	546	0.7623775	
5164	546	0.7623775	rmlC
2434	546	0.7623775	
149	546	0.7623775	
1674	546	0.7623775	folE2
171	543	0.7604938	
1481	543	0.7604938	ccmG
3726	540	0.7585952	
4251	540	0.7585952	rplE
1768	540	0.7585952	
937	540	0.7585952	
6	537	0.7566815	
5557	537	0.7566815	atpH
3396	537	0.7566815	nosL
4841	537	0.7566815	
2971	537	0.7566815	
4962	537	0.7566815	
4248	534	0.7547527	rplF
1377	534	0.7547527	
1885	534	0.7547527	
4275	534	0.7547527	nusG
4649	534	0.7547527	
2985	534	0.7547527	
1154	534	0.7547527	
5111	531	0.7528085	gloA3
4765	531	0.7528085	omlA
3575	531	0.7528085	
4031	528	0.750849	ppa
1300	528	0.750849	
2733	528	0.750849	
4460	528	0.750849	
3905	528	0.750849	
3744	528	0.750849	rimM
1867	528	0.750849	
2455	528	0.750849	
514	525	0.7488739	nirL
4965	525	0.7488739	
2464	525	0.7488739	

3095	525	0.7488739	xcpZ
2136	525	0.7488739	
1134	522	0.7468831	
1062	522	0.7468831	
1442	522	0.7468831	
3693	522	0.7468831	
3811	522	0.7468831	hscB
145	519	0.7448766	
1845	519	0.7448766	
3100	519	0.7448766	xcpU
4866	519	0.7448766	
5039	519	0.7448766	aroK
2496	516	0.7428542	
3911	516	0.7428542	
4050	516	0.7428542	pgpA
1610	516	0.7428542	fabA
3287	516	0.7428542	
403	513	0.7408157	pyrR
1514	510	0.7387611	
4114	510	0.7387611	
4559	510	0.7387611	lspA
47	510	0.7387611	
4104	510	0.7387611	
3965	510	0.7387611	
2184	510	0.7387611	
1912	507	0.7366902	
1657	507	0.7366902	
1666	507	0.7366902	
55	507	0.7366902	
3647	507	0.7366902	
973	507	0.7366902	
585	507	0.7366902	
2859	507	0.7366902	greB
350	507	0.7366902	folA
3288	504	0.7346029	
1967	501	0.732499	
4272	501	0.732499	rplJ
4246	501	0.732499	rpsE
3318	501	0.732499	
3756	501	0.732499	
2226	501	0.732499	
2645	501	0.732499	nuoJ
2367	498	0.7303785	
1837	498	0.7303785	
261	498	0.7303785	
4232	498	0.7303785	ssb
1035	495	0.7282411	
5128	492	0.7260868	secB
3815	492	0.7260868	
1173	492	0.7260868	napB
1176	492	0.7260868	napF
1772	489	0.7239154	

4211	489	0.7239154	
1900	489	0.7239154	
1899	489	0.7239154	
1745	489	0.7239154	
1956	489	0.7239154	
4210	489	0.7239154	
4574	489	0.7239154	
2517	489	0.7239154	xyfY
4728	489	0.7239154	folK
3403	486	0.7217268	
837	486	0.7217268	slyD
2768	483	0.7195209	
3856	483	0.7195209	
4295	483	0.7195209	
2797	483	0.7195209	
3918	483	0.7195209	moaC
3982	483	0.7195209	
4773	483	0.7195209	
5247	483	0.7195209	
5222	483	0.7195209	
5385	480	0.7172975	
4052	480	0.7172975	nusB
363	480	0.7172975	coaD
2935	480	0.7172975	
2461	480	0.7172975	
2819	480	0.7172975	
2721	480	0.7172975	
698	480	0.7172975	
336	480	0.7172975	
4395	480	0.7172975	
3207	480	0.7172975	
1464	480	0.7172975	
1026	477	0.7150564	
714	477	0.7150564	
2205	477	0.7150564	
4053	477	0.7150564	ribE
5081	477	0.7150564	
3785	477	0.7150564	
1696	477	0.7150564	pscO
1924	477	0.7150564	
4718	477	0.7150564	
808	474	0.7127976	
4644	474	0.7127976	
1593	474	0.7127976	
5246	474	0.7127976	
4454	474	0.7127976	
1008	474	0.7127976	bcp
1039	474	0.7127976	
116	474	0.7127976	
1206	474	0.7127976	
3627	474	0.7127976	
3302	471	0.7105208	

5558	471	0.7105208	atpF
4267	471	0.7105208	rpsG
2052	471	0.7105208	cynS
4847	471	0.7105208	accB
962	471	0.7105208	
2171	471	0.7105208	
4948	468	0.7082261	
332	468	0.7082261	
4107	468	0.7082261	
1482	468	0.7082261	ccmH
4183	468	0.7082261	
2427	468	0.7082261	
2786	468	0.7082261	
953	465	0.7059131	
4564	465	0.7059131	
2731	465	0.7059131	
4464	465	0.7059131	ptsN
80	465	0.7059131	
4057	465	0.7059131	
2978	465	0.7059131	ptpA
1306	462	0.7035818	
3616	462	0.7035818	
1673	462	0.7035818	
3470	459	0.701232	
3380	459	0.701232	
4746	459	0.701232	
5229	459	0.701232	
3320	456	0.6988636	
2499	456	0.6988636	
3309	456	0.6988636	
4828	456	0.6988636	
59	456	0.6988636	osmC
5321	456	0.6988636	dut
4421	456	0.6988636	
4697	453	0.6964764	
2538	453	0.6964764	
2829	453	0.6964764	
3916	453	0.6964764	moaE
3435	453	0.6964764	
115	453	0.6964764	
578	450	0.6940703	
678	450	0.6940703	
4525	450	0.6940703	pilA
1285	450	0.6940703	
614	450	0.6940703	
822	447	0.6916451	
245	447	0.6916451	aroQ2
1815	447	0.6916451	mhA
1594	447	0.6916451	
4630	444	0.6892007	
1122	444	0.6892007	
3067	444	0.6892007	

1105	444	0.6892007	fliJ
970	441	0.6867369	tolR
2982	441	0.6867369	
3645	441	0.6867369	fabZ
61	438	0.6842536	
1835	438	0.6842536	
5178	438	0.6842536	
1618	438	0.6842536	
2577	438	0.6842536	
3017	438	0.6842536	
2775	438	0.6842536	
1710	438	0.6842536	exsC
3341	435	0.6817506	
94	435	0.6817506	
2436	435	0.6817506	
4244	435	0.6817506	rplO
2756	435	0.6817506	
404	435	0.6817506	
4610	435	0.6817506	
250	435	0.6817506	
4767	435	0.6817506	
433	435	0.6817506	
2675	435	0.6817506	
720	435	0.6817506	
679	432	0.6792278	
3807	432	0.6792278	ndk
4274	432	0.6792278	rplK
3986	432	0.6792278	
52	429	0.6766849	
4433	429	0.6766849	rplM
1560	429	0.6766849	
2282	429	0.6766849	
2120	429	0.6766849	
4169	429	0.6766849	
5116	426	0.6741219	
2368	426	0.6741219	
2673	426	0.6741219	
700	426	0.6741219	
5553	426	0.6741219	atpC
2187	426	0.6741219	
3332	426	0.6741219	
4518	426	0.6741219	
2894	423	0.6715386	
653	423	0.6715386	
661	423	0.6715386	
542	420	0.6689348	
5130	420	0.6689348	
5465	420	0.6689348	
4935	420	0.6689348	rpsF
850	420	0.6689348	
2225	417	0.6663104	
4874	417	0.6663104	

5061	417	0.6663104	
1468	417	0.6663104	
264	417	0.6663104	
3962	417	0.6663104	
868	414	0.6636651	
5182	414	0.6636651	
1353	414	0.6636651	
2192	414	0.6636651	
3289	414	0.6636651	
4256	414	0.6636651	rplP
3558	414	0.6636651	
2674	411	0.6609989	
3611	411	0.6609989	
5300	411	0.6609989	cycB
2769	411	0.6609989	
3960	408	0.6583116	
1203	408	0.6583116	
5569	408	0.6583116	mpA
4427	408	0.6583116	sspB
1129	408	0.6583116	
1465	408	0.6583116	
1645	408	0.6583116	
1659	408	0.6583116	
4764	405	0.6556029	fur
778	405	0.6556029	
474	405	0.6556029	
5404	405	0.6556029	
398	405	0.6556029	
2016	405	0.6556029	
1883	399	0.650121	
5144	399	0.650121	
2827	399	0.650121	
2107	399	0.650121	
5543	399	0.650121	
3674	399	0.650121	
4778	399	0.650121	
1358	399	0.650121	
2706	396	0.6473475	
1250	396	0.6473475	aprl
710	396	0.6473475	gloA2
3788	396	0.6473475	
42	396	0.6473475	
2375	396	0.6473475	
5195	396	0.6473475	
4405	396	0.6473475	
2605	396	0.6473475	
3904	396	0.6473475	
4471	396	0.6473475	
4249	393	0.6445519	rpsH
5347	393	0.6445519	
4125	393	0.6445519	hpcD
4432	393	0.6445519	rpsI

3967	393	0.6445519	
2722	393	0.6445519	
5328	390	0.6417342	
4240	390	0.6417342	rpsK
4237	390	0.6417342	rplQ
4747	390	0.6417342	secG
1817	390	0.6417342	
3432	390	0.6417342	
3884	387	0.6388941	
3813	387	0.6388941	iscU
1581	387	0.6388941	sdhC
540	387	0.6388941	
3021	387	0.6388941	
4383	384	0.6360315	
4392	384	0.6360315	
2446	384	0.6360315	gcvH2
5566	384	0.6360315	
3869	384	0.6360315	
1160	384	0.6360315	
3906	384	0.6360315	
867	384	0.6360315	
4731	381	0.6331462	panD
1355	381	0.6331462	
3041	381	0.6331462	
5339	381	0.6331462	
880	381	0.6331462	
1095	381	0.6331462	
5561	381	0.6331462	atpl
591	381	0.6331462	
1518	381	0.6331462	
170	381	0.6331462	
4603	381	0.6331462	
3123	378	0.6302381	
4424	378	0.6302381	
4586	378	0.6302381	
3178	378	0.6302381	
991	378	0.6302381	
4059	378	0.6302381	
4485	378	0.6302381	
5381	378	0.6302381	
908	375	0.6273069	
2490	375	0.6273069	
680	375	0.6273069	
2753	375	0.6273069	
1456	375	0.6273069	cheY
3012	375	0.6273069	
4076	375	0.6273069	
4315	375	0.6273069	mvaT
3439	372	0.6243525	folX
4268	372	0.6243525	rpsL
5333	372	0.6243525	
2898	369	0.6213746	

5533	369	0.6213746	
1541	369	0.6213746	
4253	369	0.6213746	rplN
3833	369	0.6213746	
1149	369	0.6213746	
4271	369	0.6213746	rplL
4276	369	0.6213746	secE
1582	369	0.6213746	sdhD
2166	366	0.6183732	
33	366	0.6183732	
1701	366	0.6183732	
1842	363	0.6153479	
1378	363	0.6153479	
3203	363	0.6153479	
1840	363	0.6153479	
3843	363	0.6153479	
1076	363	0.6153479	
630	363	0.6153479	
613	360	0.6122987	
2901	360	0.6122987	
2606	360	0.6122987	
4324	360	0.6122987	
2868	360	0.6122987	
1492	357	0.6092253	
4005	357	0.6092253	
2741	357	0.6092253	rplT
2666	357	0.6092253	
1426	357	0.6092253	
4241	357	0.6092253	rpsM
2960	357	0.6092253	pilZ
871	357	0.6092253	phhB
1995	357	0.6092253	
2667	354	0.6061275	
5303	354	0.6061275	
582	354	0.6061275	folB
1568	354	0.6061275	
2736	354	0.6061275	
563	354	0.6061275	
1349	351	0.6030052	
665	351	0.6030052	
4247	351	0.6030052	rplR
320	351	0.6030052	
3742	351	0.6030052	rplS
3835	351	0.6030052	
1228	351	0.6030052	
2175	348	0.5998581	
729	348	0.5998581	
570	348	0.5998581	
1720	348	0.5998581	pscG
4711	348	0.5998581	
3684	348	0.5998581	
4702	348	0.5998581	

3664	348	0.5998581	
1917	348	0.5998581	
2190	345	0.5966861	
2762	345	0.5966861	
3688	345	0.5966861	
2780	345	0.5966861	
3046	345	0.5966861	
4739	345	0.5966861	
1398	342	0.5934889	
128	342	0.5934889	
4575	342	0.5934889	
2456	342	0.5934889	
2781	342	0.5934889	
2715	339	0.5902664	
5288	339	0.5902664	glnK
3809	339	0.5902664	fdx2
3822	339	0.5902664	
1055	339	0.5902664	
1722	339	0.5902664	pscl
3367	339	0.5902664	
565	339	0.5902664	
2608	336	0.5870183	
1965	336	0.5870183	
644	336	0.5870183	
825	336	0.5870183	
1114	336	0.5870183	
5275	336	0.5870183	
5067	336	0.5870183	hisE
589	333	0.5837445	
4258	333	0.5837445	rplV
4990	333	0.5837445	
1323	333	0.5837445	
5406	333	0.5837445	
3979	333	0.5837445	
3140	330	0.5804447	
2405	330	0.5804447	
1540	330	0.5804447	
3275	330	0.5804447	
4698	330	0.5804447	
1702	330	0.5804447	
3040	330	0.5804447	
939	327	0.5771188	
1925	327	0.5771188	
1780	327	0.5771188	nirD
4577	327	0.5771188	
3533	327	0.5771188	
2694	327	0.5771188	
5240	327	0.5771188	trxA
617	327	0.5771188	
1533	327	0.5771188	
4164	327	0.5771188	
1882	324	0.5737665	

3351	324	0.5737665	
894	324	0.5737665	
3042	324	0.5737665	
1362	324	0.5737665	
3812	324	0.5737665	iscA
802	324	0.5737665	
4853	324	0.5737665	fis
2384	324	0.5737665	
488	321	0.5703877	
1123	321	0.5703877	
1676	321	0.5703877	
1168	321	0.5703877	
5417	321	0.5703877	soxD
3502	318	0.566982	
1038	318	0.566982	
15	318	0.566982	
2422	315	0.5635494	
3854	315	0.5635494	
610	315	0.5635494	prtN
4252	315	0.5635494	rplX
2658	315	0.5635494	
1830	315	0.5635494	
4753	315	0.5635494	
922	315	0.5635494	
2759	315	0.5635494	
5227	315	0.5635494	
4264	312	0.5600895	rpsJ
3260	312	0.5600895	
4568	312	0.5600895	rplU
742	309	0.5566022	
2937	309	0.5566022	
2646	309	0.5566022	nuoK
979	309	0.5566022	
4463	309	0.5566022	
4452	309	0.5566022	
2174	309	0.5566022	
1937	309	0.5566022	
786	306	0.5530873	
3142	306	0.5530873	
4674	306	0.5530873	
3347	306	0.5530873	
2161	306	0.5530873	
4230	306	0.5530873	pchB
2245	306	0.5530873	
4789	306	0.5530873	
4250	306	0.5530873	rpsN
2607	306	0.5530873	
857	306	0.5530873	bolA
466	303	0.5495445	
3390	303	0.5495445	
647	303	0.5495445	
3298	303	0.5495445	

2738	303	0.5495445	himA
4354	303	0.5495445	
3278	300	0.5459736	
4261	300	0.5459736	rplW
2029	300	0.5459736	
4141	300	0.5459736	
3202	300	0.5459736	
2799	300	0.5459736	
2460	297	0.5423744	
1929	297	0.5423744	
709	297	0.5423744	
4875	297	0.5423744	
1705	297	0.5423744	pcrG
3662	294	0.5387467	
4419	294	0.5387467	ftsL
4386	294	0.5387467	groES
3566	294	0.5387467	
1295	294	0.5387467	
490	294	0.5387467	
900	291	0.5350903	
4482	291	0.5350903	gatC
369	291	0.5350903	
4642	291	0.5350903	
3338	291	0.5350903	
4638	288	0.5314048	
2143	288	0.5314048	
983	288	0.5314048	
131	288	0.5314048	
3274	288	0.5314048	
980	285	0.5276901	
3634	285	0.5276901	
3161	285	0.5276901	himD
4298	285	0.5276901	
2183	285	0.5276901	
3998	282	0.523946	
3051	282	0.523946	
124	282	0.523946	
2292	282	0.523946	
3940	282	0.523946	
4176	282	0.523946	ppiC2
2697	282	0.523946	
1641	279	0.5201722	
3033	279	0.5201722	
1988	279	0.5201722	pqqD
1996	279	0.5201722	ppiC1
2485	279	0.5201722	
4060	279	0.5201722	
2723	279	0.5201722	
4637	279	0.5201722	
4018	276	0.5163685	
4563	276	0.5163685	rpsT
909	276	0.5163685	

4259	276	0.5163685	rpsS
68	276	0.5163685	
954	276	0.5163685	
1852	276	0.5163685	
1298	276	0.5163685	
5148	273	0.5125346	
734	273	0.5125346	
4466	273	0.5125346	
2487	273	0.5125346	
818	273	0.5125346	
2182	270	0.5086704	
1447	270	0.5086704	fliQ
4033	270	0.5086704	
4741	270	0.5086704	rpsO
4870	267	0.5047755	
3413	267	0.5047755	
4254	267	0.5047755	rpsQ
874	267	0.5047755	
1963	267	0.5047755	
2805	264	0.5008497	
3601	264	0.5008497	
3085	264	0.5008497	
986	264	0.5008497	
1151	264	0.5008497	imm2
1508	261	0.4968928	
712	258	0.4929045	
1968	258	0.4929045	
2663	258	0.4929045	
1719	258	0.4929045	pscF
5559	258	0.4929045	atpE
1233	258	0.4929045	
384	258	0.4929045	
4567	258	0.4929045	rpmA
2737	258	0.4929045	
635	255	0.4888847	
5129	255	0.4888847	grx
1394	255	0.4888847	
4611	255	0.4888847	
53	255	0.4888847	
2031	255	0.4888847	
3245	255	0.4888847	minE
3917	252	0.4848329	moaD
2853	252	0.4848329	oprl
1063	252	0.4848329	
3745	252	0.4848329	rpsP
362	252	0.4848329	fdx1
1006	252	0.4848329	
4944	249	0.4807491	
493	249	0.4807491	
5068	249	0.4807491	tatA
3632	249	0.4807491	
4782	246	0.4766328	

2429	246	0.4766328	
1711	246	0.4766328	
2297	246	0.4766328	
738	246	0.4766328	
4134	243	0.472484	
4377	243	0.472484	
1431	243	0.472484	rsaL
4357	243	0.472484	
2149	243	0.472484	
1849	243	0.472484	
1869	240	0.4683022	
1564	240	0.4683022	
3334	240	0.4683022	
1743	240	0.4683022	
2621	237	0.4640873	
1592	237	0.4640873	
5316	237	0.4640873	rpmB
2966	237	0.4640873	acpP
2845	234	0.459839	
3009	234	0.459839	
60	234	0.459839	
2703	234	0.459839	
505	231	0.455557	
4934	231	0.455557	rpsR
648	231	0.455557	
632	231	0.455557	
1404	228	0.451241	
805	228	0.451241	
125	228	0.451241	
39	228	0.451241	
2992	228	0.451241	
4359	228	0.451241	
2021	225	0.4468909	
3530	222	0.4425063	
2453	222	0.4425063	
1855	222	0.4425063	
3612	222	0.4425063	
3031	222	0.4425063	
4028	222	0.4425063	
3237	222	0.4425063	
2785	219	0.4380869	
3501	219	0.4380869	
2412	219	0.4380869	
2619	219	0.4380869	infA
4306	219	0.4380869	
4826	219	0.4380869	
38	216	0.4336324	
4737	216	0.4336324	
579	216	0.4336324	rpsU
717	213	0.4291427	
3049	213	0.4291427	rmf
5526	213	0.4291427	

5460	213	0.4291427	
200	213	0.4291427	
2763	210	0.4246174	
1548	210	0.4246174	
2170	210	0.4246174	
456	210	0.4246174	
4823	210	0.4246174	
109	210	0.4246174	
960	210	0.4246174	
2668	210	0.4246174	
1159	210	0.4246174	
3266	210	0.4246174	capB
3451	210	0.4246174	
627	207	0.4200562	
5403	207	0.4200562	
4077	207	0.4200562	
1718	204	0.4154588	pseE
4530	201	0.410825	
380	201	0.410825	
553	201	0.410825	
3808	201	0.410825	
1936	201	0.410825	
4738	198	0.4061544	
1230	198	0.4061544	
3520	195	0.4014469	
3752	195	0.4014469	
5480	195	0.4014469	
2742	195	0.4014469	rpmI
2808	192	0.396702	
4255	192	0.396702	rpmC
1747	189	0.3919195	
905	186	0.3870991	csrA
3371	186	0.3870991	
258	186	0.3870991	
2980	186	0.3870991	
4940	186	0.3870991	
284	183	0.3822405	
2970	183	0.3822405	rpmF
1571	180	0.3773433	
3496	180	0.3773433	
1478	177	0.3724074	
5408	177	0.3724074	
3572	177	0.3724074	
4245	177	0.3724074	rpmD
2186	171	0.3624178	
4537	171	0.3624178	
2501	168	0.3573635	
2883	168	0.3573635	
1177	168	0.3573635	napE
5351	168	0.3573635	
5350	168	0.3573635	
2146	168	0.3573635	

3719	162	0.3471344	
5482	162	0.3471344	
2311	159	0.341959	
567	159	0.341959	
161	153	0.3314847	
3600	153	0.3314847	
3990	153	0.3314847	
3370	147	0.3208437	
135	141	0.3100333	
5276	141	0.3100333	lppL
1664	141	0.3100333	
5570	135	0.2990509	rpmH
3144	120	0.2708239	
442	117	0.2650435	
4242	117	0.2650435	rpmJ
1632	90	0.210914	kdpF
1985	72	0.1726306	pqqA

Protein Name
DNA-directed RNA polymerase beta* chain
DNA-directed RNA polymerase beta chain
DNA polymerase III, alpha chain
ribonucleoside reductase, large chain
valyl-tRNA synthetase
isoleucyl-tRNA synthetase
organic solvent tolerance protein OstA precursor
DNA gyrase subunit A
secretion protein SecA
alanyl-tRNA synthetase
leucyl-tRNA synthetase
aconitate hydratase 2
DNA topoisomerase I
translation initiation factor IF-2
cell division protein FtsK
DNA gyrase subunit B
Lon protease
probable outer membrane protein
DNA ligase
phenylalanyl-tRNA synthetase, beta subunit
probable chemotaxis sensor/effector fusion protein
topoisomerase IV subunit A
primosomal protein N'
hypothetical protein
hypothetical protein
elongation factor G
polyribonucleotide nucleotidyltransferase
glycyl-tRNA synthetase beta chain
DNA polymerase subunits gamma and tau
methionyl-tRNA synthetase
ATP-dependent DNA helicase Rep
hypothetical protein
cytochrome C-type biogenesis protein CcmF
probable chemotaxis transducer
threonyl-tRNA synthetase
probable heat shock protein (hsp90 family)
heat shock protein HtpG
probable acetyltransferase
topoisomerase IV subunit B
1-deoxyxylulose-5-phosphate synthase
hypothetical protein
secretion protein SecD
heat shock protein HscA
probable binding protein component of ABC transporter
glucosamine--fructose-6-phosphate aminotransferase
transport protein MsbA
GTP-binding protein LepA
probable acyl-CoA dehydrogenase
succinate dehydrogenase (A subunit)
arginyl-tRNA synthetase
probable sodium/proton antiporter

probable acetyltransferase
penicillin-binding protein 3
conserved hypothetical protein
probable oxidoreductase
acetolactate synthase large subunit
single-stranded-DNA-specific exonuclease RecJ
prolyl-tRNA synthetase
urease alpha subunit
type 4 fimbrial biogenesis protein PilB
30S ribosomal protein S1
glutamyl-tRNA synthetase
glucose-6-phosphate isomerase
hypothetical protein
electron transfer flavoprotein-ubiquinone oxidoreductase
GroEL protein
CTP synthase
probable chemotaxis transducer
arylsulfatase
conserved hypothetical protein
GMP synthase
hypothetical protein
probable carbohydrate kinase
phosphoglycerate mutase
conserved hypothetical protein
chromosomal replication initiator protein DnaA
ATP synthase alpha chain
hypothetical protein
apolipoprotein N-acyltransferase
hypothetical protein
xylulose kinase
general secretion pathway protein E
sodium/proton antiporter NhaB
probable colicin-like toxin
methylmalonate-semialdehyde dehydrogenase
RNA polymerase sigma-54 factor
probable transporter
N utilization substance protein A
hypothetical protein
probable flavin-binding monooxygenase
conserved hypothetical protein
UDP-N-acetylmuramoylalanyl-D-glutamate-2, 6-diaminopimelate ligase
hypothetical protein
probable amidase
outer membrane protein OprM precursor
RND divalent metal cation efflux membrane fusion protein CzcB precursor
Glu-tRNA(Gln) amidotransferase subunit A
pyruvate kinase II
probable Mg transporter MgtE
Glu-tRNA(Gln) amidotransferase subunit B
UDP-N-acetylmuramate-alanine ligase
lipoamide dehydrogenase-glc
probable transporter (membrane subunit)

conserved hypothetical protein
probable outer membrane protein
probable ferredoxin
glutamine synthetase
probable type II secretion system protein
nitrite extrusion protein 2
probable amidase
soluble pyridine nucleotide transhydrogenase
replicative DNA helicase
probable glyceraldehyde-3-phosphate dehydrogenase
cysteinyl-tRNA synthetase
exodeoxyribonuclease VII large subunit
UDP-N-acetylmuramoylalanyl-D-glutamyl-2, 6-diaminopimelate--D-alanyl-D-alanyl ligase
ATP synthase beta chain
signal recognition particle protein Ffh
adenylosuccinate lyase
signal recognition particle receptor FtsY
probable 2-isopropylmalate synthase
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable dicarboxylate transporter
biotin carboxylase
tryptophanyl-tRNA synthetase
UDP-N-acetylmuramoylalanine--D-glutamate ligase
NADH dehydrogenase I chain F
probable aldolase
hypothetical protein
two-component response regulator PilR
phosphoglucosamine mutase
aminopeptidase P
probable cytochrome P450
conserved hypothetical protein
secretion protein SecY
hypothetical protein
probable MFS transporter
hypothetical protein
probable MFS transporter
porin O precursor
B-band O-antigen polymerase
conserved hypothetical protein
probable UDP-glucose/GDP-mannose dehydrogenase WbpA
probable binding protein component of ABC maltose/mannitol transporter
C4-dicarboxylate transport protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
TolB protein
hypothetical protein
adenylosuccinate synthetase
peptidyl-prolyl cis-trans isomerase SurA
enolase

hypothetical protein
glutamate-1-semialdehyde 2,1-aminomutase
seryl-tRNA synthetase
3-deoxy-D-manno-octulosonic-acid (KDO) transferase
hypothetical protein
3-oxoacyl-acyl carrier protein synthase II
glutamyl-tRNA reductase
UDP-N-acetylglucosamine 1-carboxyvinyltransferase
hypothetical protein
transcription termination factor Rho
cell division protein FtsA
hypothetical protein
conserved hypothetical protein
ribonucleoside reductase, small chain
probable glycosyl transferase WbpJ
hypothetical protein
aspartate kinase alpha and beta chain
O-antigen translocase
hypothetical protein
hypothetical protein
probable transporter (membrane subunit)
conserved hypothetical protein
probable MFS transporter
conserved hypothetical protein
probable hydrolase
hypothetical protein
GTP-binding protein Obg
probable FAD-dependent monooxygenase
hypothetical protein
phenazine biosynthesis protein PhzC
probable type II secretion system protein
probable MFS transporter
conserved hypothetical protein
nitrate transporter
probable cytochrome b
hypothetical protein
DNA/pantothenate metabolism flavoprotein
membrane protein OpdE
two-component sensor
probable acyl-CoA thiolase
8-amino-7-oxononanoate synthase
conserved hypothetical protein
cell division protein FtsW
hypothetical protein
probable FAD-dependent monooxygenase
conserved hypothetical protein
probable MFS transporter
probable acyl-CoA thiolase
hypothetical protein
1-deoxy-d-xylulose 5-phosphate reductoisomerase
methionine adenosyltransferase
cell division protein FtsZ

hypothetical protein
probable pyridoxal-phosphate dependent enzyme
acetyl-CoA acetyltransferase
probable molybdopterin biosynthesis protein MoeB
conserved hypothetical protein
hypothetical protein
alginate biosynthesis protein Alg44
hypothetical protein
probable hydrolase
succinyl-CoA synthetase beta chain
hypothetical protein
probable ATP-binding component of ABC transporter
probable acyl-CoA dehydrogenase
phosphoglycerate kinase
hypothetical protein
hypothetical protein
probable RND efflux membrane fusion protein precursor
probable peptidic bond hydrolase
probable multidrug resistance efflux pump
succinyl-diaminopimelate desuccinylase
conserved hypothetical protein
probable acyl-CoA dehydrogenase
general secretion pathway protein L
probable permease of ABC transporter
erythronate-4-phosphate dehydrogenase
conserved hypothetical protein
hypothetical protein
probable acyl-CoA thiolase
conserved hypothetical protein
lipid A-disaccharide synthase
LPS biosynthesis protein WbpG
hypothetical protein
tRNA methyltransferase
probable acyl-CoA dehydrogenase
conserved hypothetical protein
conserved hypothetical protein
still frameshift type 4 fimbrial biogenesis protein PilC
cytochrome c oxidase, subunit II
conserved hypothetical protein
riboflavin-specific deaminase/reductase
probable glycosyltransferase WbpH
glycine cleavage system protein T2
muconate cycloisomerase I
UDP-glucose:(heptosyl) LPS alpha 1,3-glucosyltransferase WaaG
hypothetical protein
glutamate 5-kinase
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
aspartate semialdehyde dehydrogenase
rod shape-determining protein

alcohol dehydrogenase (Zn-dependent)
conserved hypothetical protein
hypothetical protein
peptide chain release factor 2
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
3-phosphoserine aminotransferase
peptide chain release factor 1
phospho-N-acetylmuramoyl-pentapeptide-transferase
hypothetical protein
probable aminotransferase WbpE
phospho-2-dehydro-3-deoxyheptonate aldolase
O6-methylguanine-DNA methyltransferase
probable transcriptional regulator
UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine tr
uroporphyrinogen decarboxylase
hypothetical protein
heptosyltransferase I
conserved hypothetical protein
fructose-1,6-bisphosphate aldolase
type 4 fimbrial biogenesis protein PilM
probable UDP-N-acetylglucosamine 2-epimerase Wbpl
phosphoribosylaminoimidazole synthetase
UDP-3-O-[3-hydroxyauroyl] glucosamine N-acyltransferase
quinolate synthetase A
probable secretion protein
probable alcohol dehydrogenase (Zn-dependent)
conserved hypothetical protein
dTDP-D-glucose 4,6-dehydratase
outer membrane protein OprF precursor
hypothetical protein
conserved hypothetical protein
translocation protein in type III secretion
O-antigen chain length regulator
TolA protein
transcriptional regulator MexT
conserved hypothetical protein
acetylputrescine aminohydrolase
conserved hypothetical protein
RecA protein
heptosyltransferase II
hypothetical protein
conserved hypothetical protein
rod shape-determining protein MreB
hypothetical protein
DNA polymerase III, delta subunit
tetrahydrodipicolinate succinylase
probable binding protein component of ABC transporter
hypothetical protein
conserved hypothetical protein

TonB protein
O-sialoglycoprotein endopeptidase
ferrochelatase
conserved hypothetical protein
probable aminotransferase
probable transmembrane sensor
UDP-N-acetylpyruvoylglucosamine reductase
hypothetical protein
acetoin catabolism protein AcoB
conserved hypothetical protein
probable oxidoreductase
hypothetical protein
glycosyltransferase WbpL
hypothetical protein
probable transposase
flagellar motor switch protein FliG
hypothetical protein
probable transposase
probable transposase
probable transposase
probable transposase
phenylalanyl-tRNA synthetase, alpha-subunit
probable permease of ABC transporter
hypothetical protein
hypothetical protein
fructose-1,6-bisphosphatase
conserved hypothetical protein
probable ATP-binding component of ABC transporter
conserved hypothetical protein
hypothetical protein
probable O-methyltransferase
aspartate carbamoyltransferase
glyceraldehyde 3-phosphate dehydrogenase
conserved hypothetical protein
DNA-directed RNA polymerase alpha chain
probable pyruvate dehydrogenase E1 component, beta chain
tetraacyldisaccharide 4*-kinase
rod shape-determining protein MreC
D-lactate dehydrogenase (fermentative)
sulfate transport protein CysA
probable nucleoside hydrolase
pyridoxal phosphate biosynthetic protein PdxA
probable transmembrane sensor
DNA polymerase III, delta prime subunit
L-asparaginase I
hypothetical protein
probable bacteriophage integrase
lipoate synthase
hypothetical protein
conserved hypothetical protein
hypothetical protein
probable transcriptional regulator

conserved hypothetical protein
conserved hypothetical protein
delta 2-isopentenylpyrophosphate transferase
octaprenyl-diphosphate synthase
hypothetical protein
hypothetical protein
probable enoyl-CoA hydratase/isomerase
thiamine monophosphate kinase
hypothetical protein
hypothetical protein
hypothetical protein
probable serine/threonine dehydratase, degradative
pseudouridine synthase
conserved hypothetical protein
hypothetical protein
ribosomal large subunit pseudouridine synthase C
probable transcriptional regulator
hypothetical protein
probable transmembrane sensor
hypothetical protein
probable transcriptional regulator
probable transcriptional regulator
glutathione synthetase
hypothetical protein
probable adhesion protein
acetyl-coenzyme A carboxylase carboxyl transferase (alpha subunit)
probable transcriptional regulator
probable NAD-dependent epimerase/dehydratase WbpK
probable oxidoreductase WpbB
probable transmembrane sensor
hypothetical protein
glycyl-tRNA synthetase alpha chain
probable lipase
LytB protein
conserved hypothetical protein
probable hydrolase
ribose-phosphate pyrophosphokinase
hypothetical protein
conserved hypothetical protein
porphobilinogen deaminase
probable transcriptional regulator
probable lauroyl acyltransferase
transcriptional regulator PtxR
probable transcriptional regulator
hypothetical protein
malonyl-CoA-[acyl-carrier-protein] transacylase
riboflavin kinase/FAD synthase
conserved hypothetical protein
conserved hypothetical protein
probable phosphatidate cytidylyltransferase
hypothetical protein
carbamate kinase

hypothetical protein
probable transcriptional regulator
catechol 1,2-dioxygenase
D-alanyl-D-alanine-endopeptidase
probable transcriptional regulator
hypothetical protein
probable epimerase
lipase LipC
probable transcriptional regulator
electron transfer flavoprotein alpha-subunit
FdhE protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
probable ATP-binding component of ABC transporter
probable cytochrome c
probable transcriptional regulator
hypothetical protein
probable transcriptional regulator
probable permease of ABC transporter
hypothetical protein
probable transcriptional regulator
probable transcriptional regulator
probable transcriptional regulator
GTP-binding protein Era
probable transcriptional regulator
pyrroloquinoline quinone biosynthesis protein B
probable cytochrome c oxidase assembly factor
hypothetical protein
hypothetical protein
probable short chain dehydrogenase
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
UDP-3-O-acyl-N-acetylglucosamine deacetylase
probable transcriptional regulator
probable transcriptional regulator
conserved hypothetical protein
probable binding protein component of ABC transporter
dTDP-4-dehydrorhamnose reductase
conserved hypothetical protein
probable transcriptional regulator
hypothetical protein
hypothetical protein
probable transcriptional regulator
probable transferase
probable two-component response regulator
probable transcriptional regulator
hypothetical protein
cysteine synthase B
probable glycosyl transferase

hypothetical protein
probable transcriptional regulator
probable transcriptional regulator
probable transcriptional regulator
probable transcriptional regulator
probable transcriptional regulator
cytochrome o ubiquinol oxidase protein CyoE
probable 3-hydroxyisobutyrate dehydrogenase
probable transcriptional regulator
4-hydroxybenzoate-octaprenyl transferase
probable chemotaxis protein
conserved hypothetical protein
probable 2-OH-lauroyltransferase
probable transcriptional regulator
succinyl-CoA synthetase alpha chain
conserved hypothetical protein
geranyltranstransferase
hypothetical protein
ribosomal protein L11 methyltransferase
glucose-1-phosphate thymidyltransferase
conserved hypothetical protein
hypothetical protein
dihydrodipicolinate synthase
heat shock protein HtpX
methyltransferase PilK
probable transcriptional regulator
conserved hypothetical protein
hypothetical protein
chromosome partitioning protein Spo0J
hypothetical protein
acetyl-CoA carboxylase beta subunit
elongation factor Ts
cell division protein ZipA
ATP synthase A chain
outer membrane protein PopN
lipase modulator protein
hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
hypothetical protein
cell division protein FtsQ
malonate decarboxylase beta subunit
ATP synthase gamma chain
probable hydrolase
hypothetical protein
probable short-chain dehydrogenase
spermidine synthase
probable ATP-binding component of ABC transporter
hypothetical protein
hypothetical protein
probable ATP-binding component of ABC transporter
hypothetical protein

probable transcriptional regulator
5,10-methylene-tetrahydrofolate dehydrogenase / cyclohydrolase
sigma factor RpoH
signal peptidase I
hypothetical protein
formyltetrahydrofolate deformylase
dihydropteroate synthase
conserved hypothetical protein
probable potassium channel
isopentenyl monophosphate kinase
hypothetical protein
hypothetical protein
nicotinate-nucleotide pyrophosphorylase
conserved hypothetical protein
hypothetical protein
2-dehydro-3-deoxyphosphooctonate aldolase
probable transmembrane sensor
urease accessory protein
flagellar synthesis regulator FlaN
probable ATP-binding component of ABC transporter
probable phenazine biosynthesis protein
ATP-binding component of ABC phosphonate transporter
probable ATP-binding component of ABC transporter
probable permease of ABC transporter
probable short-chain dehydrogenase
diaminopimelate epimerase
probable two-component response regulator
conserved hypothetical protein
NH ₃ -dependent NAD synthetase
NosY protein
probable biotin synthesis protein BioC
probable transcriptional regulator
type 4 fimbrial biogenesis protein PilW
probable chemotaxis protein methyltransferase
conserved hypothetical protein
50S ribosomal protein L2
hypothetical protein
probable oxidoreductase
probable permease of ABC taurine transporter
conserved hypothetical protein
hypothetical protein
hypothetical protein
phosphatidate cytidyltransferase
phosphatidylserine synthase
hypothetical protein
thiosulfate sulfurtransferase
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator

probable permease of ABC transporter
conserved hypothetical protein
probable transcriptional regulator
hypothetical protein
dihydrodipicolinate reductase
hypothetical protein
lipopolysaccharide core biosynthesis protein WaaP
tryptophan synthase alpha chain
probable ATP-binding component of ABC transporter
hypothetical protein
probable permease of ABC-2 transporter
probable transcriptional regulator
conserved hypothetical protein
prolipoprotein diacylglycerol transferase
3-methyl-2-oxobutanoate hydroxymethyltransferase
glutamate racemase
conserved hypothetical protein
probable permease of ABC transporter
probable permease of ABC transporter
probable enoyl-CoA hydratase/isomerase
probable transcriptional regulator
conserved hypothetical protein
thymidylate synthase
hypothetical protein
hypothetical protein
probable enoyl-CoA hydratase/isomerase
translocation protein in type III secretion
hypothetical protein
probable pili assembly chaperone
probable transcriptional regulator
probable plasmid partitioning protein
probable permease of ABC transporter
conserved hypothetical protein
methionine aminopeptidase
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator
probable permease of ABC-2 transporter
probable NAD(P)H dehydrogenase
conserved hypothetical protein
hypothetical protein
UDP-N-acetylglucosamine acyltransferase
ferredoxin--NADP+ reductase
probable permease of ABC transporter
conserved hypothetical protein
probable enoyl-CoA hydratase/isomerase
polyamine transport protein PotC
ubiquinone biosynthesis methyltransferase UbiE
hypothetical protein
transcriptional regulator PrtR
conserved hypothetical protein

probable transcriptional regulator
conserved hypothetical protein
probable exopolysaccharide transporter
probable ATP-binding component of ABC transporter
hypothetical protein
probable short-chain dehydrogenase
conserved hypothetical protein
3-deoxy-manno-octulosonate cytidyltransferase
probable transporter
conserved hypothetical protein
probable transcriptional regulator
probable thioesterase
hypothetical protein
hypothetical protein
hypothetical protein
cis-1,2-dihydroxycyclohexa-3,4-diene carboxylate dehydrogenase
probable enoyl-CoA hydratase/isomerase
molybdopterin biosynthesis MoeB protein
probable short-chain dehydrogenase
conserved hypothetical protein
heme exporter protein CcmC
hypothetical protein
tRNA (guanine-N1)-methyltransferase
type 4 fimbrial biogenesis protein PilF
imidazoleglycerol-phosphate synthase, cyclase subunit
conserved hypothetical protein
triosephosphate isomerase
uroporphyrinogen-III synthetase
undecaprenyl pyrophosphate synthetase
hypothetical protein
probable cobalamin biosynthetic protein
hypothetical protein
hypothetical protein
hypothetical protein
probable short-chain dehydrogenase
hypothetical protein
electron transfer flavoprotein beta-subunit
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
3-oxoacyl-[acyl-carrier-protein] reductase
hypothetical protein
hypothetical protein
probable pili assembly chaperone
DNA polymerase III, epsilon chain
30S ribosomal protein S2
hypothetical protein
hypothetical protein
probable nucleoside phosphorylase

uridylate kinase
hypothetical protein
probable permease of ABC transporter
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
transcriptional regulator RhlR
probable phosphoribosyl transferase
probable ATP-binding component of ABC transporter
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
probable biotin biosynthesis protein bioH
probable permease of ABC transporter
hypothetical protein
conserved hypothetical protein
ribonuclease PH
probable glutamine amidotransferase
conserved hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
probable transcriptional regulator
DNA-specific endonuclease I
probable transcriptional regulator
hypothetical protein
hypothetical protein
probable pili assembly chaperone
probable two-component response regulator
phosphoribosylaminoimidazole-succinocarboxamide synthase
succinate dehydrogenase (B subunit)
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
probable ATP-binding component of ABC transporter
heme exporter protein CcmA
hypothetical protein
hypothetical protein
probable transcriptional regulator
3-demethylubiquinone-9 3-methyltransferase
probable hydrolase
orotidine 5'-phosphate decarboxylase
hypothetical protein
hypothetical protein
50S ribosomal protein L1
conserved hypothetical protein
probable permease of ABC transporter

hypothetical protein
probable acetyltransferase
hypothetical protein
TolQ protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
probable pseudouridylate synthase
cytidylate kinase
hypothetical protein
two-component response regulator
30S ribosomal protein S3
hypothetical protein
probable transcriptional regulator
dethiobiotin synthase
molybdenum transport protein ModB
transcriptional regulator Dnr
hypothetical protein
probable ATP-binding component of ABC transporter
leucyl/phenylalanyl-tRNA-protein transferase
conserved hypothetical protein
NADH dehydrogenase I chain B
probable two-component response regulator
hypothetical protein
probable transcriptional regulator
Na⁺-translocating NADH:uniquinone oxidoreductase subunit Nqr4
ribonuclease T
hypothetical protein
conserved hypothetical protein
DNA repair protein RadC
ribulose-phosphate 3-epimerase
hypothetical protein
hypothetical protein
heme exporter protein CcmB
hypothetical protein
urease accessory protein UreF
ribose 5-phosphate isomerase
phosphoribosylaminoimidazole synthetase
probable transcriptional regulator
probable transcriptional regulator
probable transcriptional regulator
hypothetical protein
conserved hypothetical protein
probable acetyltransferase
probable transcriptional regulator
probable two-component response regulator
conserved hypothetical protein
2-keto-3-deoxy-6-phosphogluconate aldolase
probable permease of ABC transporter
hypothetical protein
hypothetical protein
probable transcriptional regulator

hypothetical protein
hypothetical protein
riboflavin synthase alpha chain
conserved hypothetical protein
thiopurine methyltransferase
probable permease of ABC transporter
alginate o-acetyltransferase AlgF
conserved hypothetical protein
conserved hypothetical protein
probable transcriptional regulator
pyridoxine 5'-phosphate oxidase
hypothetical protein
hypothetical protein
probable carboxylesterase
pyoverdine biosynthesis protein PvcD
probable transcriptional regulator
probable carbonic anhydrase
conserved hypothetical protein
probable pyridoxamine 5'-phosphate oxidase
probable pyridoxamine 5'-phosphate oxidase
hypothetical protein
probable glutathione S-transferase
hypothetical protein
transcriptional regulator Vfr
hypothetical protein
orotate phosphoribosyltransferase
glutamine amidotransferase
hypothetical protein
hypothetical protein
maleylacetoacetate isomerase
probable radical activating enzyme
hypothetical protein
uracil phosphoribosyltransferase
hypothetical protein
endonuclease III
probable transcriptional regulator
probable antioxidant protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
probable tolQ-type transport protein
pseudouridine synthase RluA
conserved hypothetical protein
50S ribosomal protein L3
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable two-component response regulator
thymidylate kinase
conserved hypothetical protein
conserved hypothetical protein
probable aromatic acid decarboxylase

hypothetical protein
probable nuclease
periplasmic chaperone LolA
hypothetical protein
probable oxidoreductase
hypothetical protein
hypothetical protein
cell division protein FtsJ
hypothetical protein
hypothetical protein
hypothetical protein
30S ribosomal protein S4
homoserine kinase
hypothetical protein
probable lipoprotein localization protein LolB
stringent starvation protein A
hypothetical protein
GTP cyclohydrolase II
hypothetical protein
heme acquisition protein HasA
probable transcriptional regulator
probable peptide chain release factor
probable ribosomal protein L25
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
guanylate kinase
glutamine amidotransferase
conserved hypothetical protein
hypothetical protein
protocatechuate 3,4-dioxygenase, alpha subunit
hypothetical protein
autoinducer synthesis protein LasI
probable Clp-family ATP-dependent protease
hypothetical protein
50S ribosomal protein L4
conserved hypothetical protein
probable nitroreductase
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
probable molybdopterin-guanine dinucleotide biosynthesis protein MobA
hypothetical protein
cytochrome c-type protein NapC
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable phosphoheptose isomerase

probable type II secretion system protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
type 4 fimbrial biogenesis protein PilX
conserved hypothetical protein
anti-sigma factor MucA
probable transcriptional regulator
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
peptidyl-tRNA hydrolase
hypothetical protein
superoxide dismutase
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable DNA invertase
probable acetyltransferase WbpD
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
ribosomal protein alanine acetyltransferase
probable transcriptional regulator
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
translation elongation factor P
conserved hypothetical protein
hypothetical protein
transcriptional regulator NfxB
probable transcriptional regulator
probable protease
alkyl hydroperoxide reductase subunit C
peptidyl-prolyl cis-trans isomerase A
hypothetical protein
hypothetical protein
hypothetical protein
GTP cyclohydrolase I precursor
probable transcriptional regulator
heat shock protein GrpE
CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase
conserved hypothetical protein
conserved hypothetical protein

ribosome recycling factor
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
hypothetical protein
translation initiation factor IF-3
potassium-transporting ATPase, C chain
probable transcriptional regulator
conserved hypothetical protein
conserved hypothetical protein
adenine phosphoribosyltransferase
conserved hypothetical protein
dTDP-4-dehydrorhamnose 3,5-epimerase
hypothetical protein
probable sigma-70 factor, ECF subfamily
GTP cyclohydrolase I precursor
hypothetical protein
cytochrome C biogenesis protein CcmG
conserved hypothetical protein
50S ribosomal protein L5
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
ATP synthase delta chain
NosL protein
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
50S ribosomal protein L6
conserved hypothetical protein
conserved hypothetical protein
transcription antitermination protein NusG
hypothetical protein
hypothetical protein
conserved hypothetical protein
lactoylglutathione lyase
outer membrane lipoprotein OmlA
hypothetical protein
inorganic pyrophosphatase
probable sigma-70 factor, ECF subfamily
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
16S rRNA processing protein
hypothetical protein
hypothetical protein
heme d1 biosynthesis protein NirL
hypothetical protein
hypothetical protein

general secretion pathway protein M
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
heat shock protein HscB
hypothetical protein
hypothetical protein
general secretion pathway protein H
conserved hypothetical protein
shikimate kinase
hypothetical protein
conserved hypothetical protein
phosphatidylglycerophosphatase A
beta-hydroxydecanoyl-ACP dehydrase
conserved hypothetical protein
transcriptional regulator PyrR
conserved hypothetical protein
spermidine acetyltransferase
prolipoprotein signal peptidase
hypothetical protein
conserved hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
probable sigma-70 factor, ECF subfamily
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable outer membrane protein precursor
probable outer membrane protein
hypothetical protein
transcription elongation factor GreB
dihydrofolate reductase
hypothetical protein
hypothetical protein
50S ribosomal protein L10
30S ribosomal protein S5
hypothetical protein
hypothetical protein
hypothetical protein
NADH dehydrogenase I chain J
hypothetical protein
hypothetical protein
hypothetical protein
single-stranded DNA-binding protein
hypothetical protein
secretion protein SecB
conserved hypothetical protein
cytochrome c-type protein NapB precursor
ferredoxin protein NapF
probable methyltransferase

probable phenazine biosynthesis protein
probable phenazine biosynthesis protein
probable phenazine biosynthesis protein
hypothetical protein
hypothetical protein
probable phenazine biosynthesis protein
conserved hypothetical protein
toluate 1,2-dioxygenase beta subunit
2-amino-4-hydroxy-6-hydroxymethyldihydropteridine pyrophosphokinase
hypothetical protein
peptidyl-prolyl cis-trans isomerase SlyD
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
molybdopterin biosynthetic protein C
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
NusB protein
phosphopantetheine adenylyltransferase
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
probable purine-binding chemotaxis protein
hypothetical protein
hypothetical protein
hypothetical protein
6,7-dimethyl-8-ribityllumazine synthase
hypothetical protein
conserved hypothetical protein
translocation protein in type III secretion
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
bacterioferritin comigratory protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein

ATP synthase B chain
30S ribosomal protein S7
cyanate lyase
biotin carboxyl carrier protein (BCCP)
probable dna-binding stress protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
cytochrome C-type biogenesis protein CcmH
hypothetical protein
hypothetical protein
hypothetical protein
probable thioredoxin
conserved hypothetical protein
hypothetical protein
nitrogen regulatory IIA protein
hypothetical protein
conserved hypothetical protein
phosphotyrosine protein phosphatase
probable HIT family protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
probable deaminase
conserved hypothetical protein
conserved hypothetical protein
osmotically inducible protein OsmC
deoxyuridine 5'-triphosphate nucleotidohydrolase
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
molybdopterin converting factor, large subunit
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
probable type II secretion system protein
type 4 fimbrial precursor PilA
probable transcriptional regulator
hypothetical protein
hypothetical protein
3-dehydroquinate dehydratase
ribonuclease H
hypothetical protein
hypothetical protein
probable peptide deformylase
probable transcriptional regulator

flagellar protein FliJ
TolR protein
conserved hypothetical protein
(3R)-hydroxymyristoyl-[acyl carrier protein] dehydratase
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
hypothetical protein
exoenzyme S synthesis protein C precursor
probable transcriptional regulator
hypothetical protein
hypothetical protein
50S ribosomal protein L15
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
probable type II secretion system protein
helix destabilizing protein of bacteriophage Pf1
hypothetical protein
nucleoside diphosphate kinase
50S ribosomal protein L11
hypothetical protein
hypothetical protein
50S ribosomal protein L13
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
probable transcriptional regulator
hypothetical protein
probable type II secretion system protein
hypothetical protein
ATP synthase epsilon chain
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
30S ribosomal protein S6
hypothetical protein
hypothetical protein
conserved hypothetical protein

conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
50S ribosomal protein L16
hypothetical protein
probable type II secretion system protein
hypothetical protein
cytochrome c5
hypothetical protein
hypothetical protein
hypothetical protein
ribonuclease P protein component
stringent starvation protein B
probable fosfomycin resistance protein
hypothetical protein
hypothetical protein
hypothetical protein
ferric uptake regulation protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator
probable NADH-ubiquinone/plastoquinone oxidoreductase
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator
hypothetical protein
hypothetical protein
alkaline proteinase inhibitor AprI
lactoylglutathione lyase
hypothetical protein
hypothetical protein
hypothetical protein
probable heat shock protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
30S ribosomal protein S8
hypothetical protein
5-carboxymethyl-2-hydroxymuconate isomerase
30S ribosomal protein S9

hypothetical protein	
hypothetical protein	
probable cytochrome c(mono-heme type)	
30S ribosomal protein S11	
50S ribosomal protein L17	
secretion protein SecG	
hypothetical protein	
hypothetical protein	
hypothetical protein	
probable iron-binding protein IscU	
succinate dehydrogenase (C subunit)	
hypothetical protein	
hypothetical protein	
conserved hypothetical protein	
conserved hypothetical protein	
glycine cleavage system protein H2	
hypothetical protein	
hypothetical protein	
hypothetical protein	
hypothetical protein	
hypothetical protein	
aspartate 1-decarboxylase precursor	
hypothetical protein	
hypothetical protein	
conserved hypothetical protein	
probable ring-cleaving dioxygenase	
hypothetical protein	
ATP synthase protein I	
conserved hypothetical protein	
conserved hypothetical protein	
hypothetical protein	
hypothetical protein	
conserved hypothetical protein	
conserved hypothetical protein	
hypothetical protein	
hypothetical protein	
hypothetical protein	
hypothetical protein	
conserved hypothetical protein	
hypothetical protein	
hypothetical protein	
conserved hypothetical protein	
probable type II secretion system protein	
hypothetical protein	
two-component response regulator CheY	
hypothetical protein	
hypothetical protein	
transcriptional regulator MvaT, P16 subunit	
d-erythro-7,8-dihydroneopterin triphosphate	epimerase
30S ribosomal protein S12	
conserved hypothetical protein	
hypothetical protein	

hypothetical protein
probable drug efflux transporter
50S ribosomal protein L14
hypothetical protein
hypothetical protein
50S ribosomal protein L7 / L12
secretion protein SecE
succinate dehydrogenase (D subunit)
hypothetical protein
hypothetical protein
conserved hypothetical protein in type III secretion
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
50S ribosomal protein L20
probable 6-pyruvoyl tetrahydrobiopterin synthase
hypothetical protein
30S ribosomal protein S13
type 4 fimbrial biogenesis protein PilZ
pterin-4-alpha-carbinolamine dehydratase
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
dihydroneopterin aldolase
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
50S ribosomal protein L18
conserved hypothetical protein
50S ribosomal protein L19
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
type III export protein PscG
hypothetical protein
hypothetical protein
hypothetical protein

conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
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conserved hypothetical protein
hypothetical protein
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probable ferredoxin
nitrogen regulatory protein P-II 2
ferredoxin [2Fe-2S]
conserved hypothetical protein
conserved hypothetical protein
type III export protein PscI
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
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hypothetical protein
conserved hypothetical protein
phosphoribosyl-ATP pyrophosphohydrolase
conserved hypothetical protein
50S ribosomal protein L22
SMR multidrug efflux transporter
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein in type III secretion
conserved hypothetical protein
hypothetical protein
hypothetical protein
assimilatory nitrite reductase small subunit
hypothetical protein
conserved hypothetical protein
probable thioredoxin
thioredoxin
probable bacteriophage protein
conserved hypothetical protein
hypothetical protein
probable transporter

hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable iron-binding protein IscA
hypothetical protein
DNA-binding protein Fis
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
sarcosine oxidase delta subunit
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
transcriptional regulator PrtN
50S ribosomal protein L24
hypothetical protein
hypothetical protein
conserved hypothetical protein
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conserved hypothetical protein
30S ribosomal protein S10
probable transcriptional regulator
50S ribosomal protein L21
hypothetical protein
hypothetical protein
NADH dehydrogenase I chain K
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
probable transporter
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
salicylate biosynthesis protein PchB
hypothetical protein
conserved hypothetical protein
30S ribosomal protein S14
conserved hypothetical protein
morphogene protein BofA
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein

integration host factor, alpha subunit

conserved hypothetical protein

hypothetical protein

50S ribosomal protein L23

hypothetical protein

hypothetical protein

conserved hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

regulator in type III secretion

hypothetical protein

cell division protein FtsL

GroES protein

conserved hypothetical protein

conserved hypothetical protein

hypothetical protein

hypothetical protein

Glu-tRNA(Gln) amidotransferase subunit C

hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

conserved hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

conserved hypothetical protein

integration host factor beta subunit

hypothetical protein

hypothetical protein

conserved hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

probable DNA binding protein

peptidyl-prolyl cis-trans isomerase C2

hypothetical protein

hypothetical protein

hypothetical protein

pyrroloquinoline quinone biosynthesis protein D

peptidyl-prolyl cis-trans isomerase C1

hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

hypothetical protein

30S ribosomal protein S20

hypothetical protein

30S ribosomal protein S19
hypothetical protein
probable acylphosphatase
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
probable phosphoryl carrier protein
hypothetical protein
hypothetical protein
hypothetical protein
flagellar biosynthetic protein FliQ
hypothetical protein
30S ribosomal protein S15
conserved hypothetical protein
conserved hypothetical protein
30S ribosomal protein S17
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
pyocin S2 immunity protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
type III export protein PscF
atp synthase C chain
hypothetical protein
hypothetical protein
50S ribosomal protein L27
conserved hypothetical protein
hypothetical protein
glutaredoxin
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
cell division topological specificity factor MinE
molybdopterin converting factor, small subunit
major outer membrane lipoprotein precursor
hypothetical protein
30S ribosomal protein S16
ferredoxin [4Fe-4S]
conserved hypothetical protein
conserved hypothetical protein
probable biotin-requiring enzyme
translocation protein TatA
conserved hypothetical protein
hypothetical protein

hypothetical protein
hypothetical protein
probable ferredoxin
conserved hypothetical protein
hypothetical protein
hypothetical protein
regulatory protein RsaL
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
probable acyl carrier protein
conserved hypothetical protein
probable acyl carrier protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
50S ribosomal protein L28
acyl carrier protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
30S ribosomal protein S18
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
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conserved hypothetical protein
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conserved hypothetical protein
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conserved hypothetical protein
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conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
initiation factor
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
30S ribosomal protein S21
hypothetical protein of bacteriophage Pf1
ribosome modulation factor
hypothetical protein

hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
probable cold-shock protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable cold-shock protein
cold acclimation protein B
hypothetical protein
conserved hypothetical protein
probable transcriptional regulator
probable transcriptional regulator
type III export protein PscE
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
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hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
50S ribosomal protein L35
hypothetical protein
50S ribosomal protein L29
hypothetical protein
carbon storage regulator
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
50S ribosomal protein L32
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
50S ribosomal protein L30
hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
periplasmic nitrate reductase protein NapE
rubredoxin
rubredoxin
conserved hypothetical protein

hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
lipopeptide precursor
hypothetical protein
50S ribosomal protein L34
hypothetical protein
hypothetical protein
50S ribosomal protein L36
KdpF protein
pyrroloquinoline quinone biosynthesis protein A

Mutant Name	Insertion Point	Host strain
001A01	3254036	PAK
001A03	4214526	PAK
001A04	800208	PAK
001A05	3627210	PAK
001A06	4931913	PAK
001A07	1034469	PAK
001A08	6144940	PAK
001A09	4102307	PAK
001A11	1515737	PAK
001A12	1244688	PAK
001B02	5924618	PAK
001B03	3267350	PAK
001B04	3302119	PAK
001B05	3108121	PAK
001B06	3987545	PAK
001B07	5585518	PAK
001B09	4682141	PAK
001B10	5041902	PAK
001B11	3187871	PAK
001C01	5924618	PAK
001C02	2871514	PAK
001C03	474619	PAK
001C04	515693	PAK
001C05	6155744	PAK
001C06	5741543	PAK
001C08	594556	PAK
001C09	2370763	PAK
001C10	4186878	PAK
001C11	2016482	PAK
001C12	5610441	PAK
001D01	6193619	PAK
001D03	6078034	PAK
001D04	6139878	PAK
001D05	522531	PAK
001D06	3567982	PAK
001D08	3998726	PAK
001D09	2140251	PAK
001D10	1301169	PAK
001D11	3423519	PAK
001D12	3472670	PAK
001E02	800936	PAK
001E03	4246525	PAK
001E04	477959	PAK
001E05	477959	PAK
001E06	5939777	PAK
001E07	5471284	PAK
001E08	5582311	PAK
001E09	442285	PAK
001E10	4514879	PAK
001E11	4514879	PAK
001E12	5064081	PAK

001F01	903376	PAK
001F02	1889581	PAK
001F03	1230813	PAK
001F04	5755640	PAK
001F05	5355403	PAK
001F06	4493238	PAK
001F07	850016	PAK
001F08	5286479	PAK
001F09	3035834	PAK
001F10	270414	PAK
001F11	4300290	PAK
001F12	3471740	PAK
001G01	5431778	PAK
001G06	5064081	PAK
001G07	353196	PAK
001G08	4881356	PAK
001G09	4684466	PAK
001G10	1340542	PAK
001G11	2659761	PAK
001G12	4553600	PAK
001GO1	5431778	PAK
001GO2	627197	PAK
001GO3	3005616	PAK
001GO5	2300131	PAK
001GO6	5064081	PAK
001GO7	353195	PAK
001GO8	4881356	PAK
001GO9	4684465	PAK
001H01	4600925	PAK
001H02	4465691	PAK
001H03	435295	PAK
001H04	5583961	PAK
001H06	5823734	PAK
001H08	3880466	PAK
001H09	271720	PAK
001H10	433381	PAK
001H11	395319	PAK
002A01	3652524	PAK
002A02	3987593	PAK
002A03	530429	PAK
002A04	6232877	PAK
002A05	1543845	PAK
002A06	619210	PAK
002A07	4795351	PAK
002A09	1152202	PAK
002A10	1205010	PAK
002A11	449470	PAK
002B01	5643797	PAK
002B02	3423910	PAK
002B03	3616916	PAK
002B04	1511758	PAK
002B05	3809953	PAK

002B06	1277931	PAK
002B07	1277942	PAK
002B08	5436760	PAK
002B09	1030806	PAK
002B10	1030806	PAK
002B11	3355560	PAK
002B12	3935624	PAK
003A01	2016406	PAK
003A02	4987284	PAK
003A03	1713832	PAK
003A04	1859681	PAK
003A05	433381	PAK
003A06	6241260	PAK
003A08	1026213	PAK
003A09	4822426	PAK
003A10	513656	PAK
003A11	5050248	PAK
003B04	3377875	PAK
003B06	1969305	PAK
003B07	433381	PAK
003B08	1034469	PAK
003B09	5907415	PAK
003B10	4192241	PAK
003B11	4192241	PAK
003C01	5713913	PAK
003C02	2609592	PAK
003C03	2095164	PAK
003C04	5369447	PAK
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003C07	2410828	PAK
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003C09	3998623	PAK
003C10	3771149	PAK
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003D01	433382	PAK
003D02	259586	PAK
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003D04	433381	PAK
003D05	4893664	PAK
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003D08	433381	PAK
003D09	5970386	PAK
003D12	2049456	PAK
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003E06	5415888	PAK
003E07	5929820	PAK
003E08	5414529	PAK
003E09	835119	PAK
003E10	4855368	PAK
003E12	5159655	PAK

003F01	683274	PAK
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003F04	4638260	PAK
003F05	2695523	PAK
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003H06	3266054	PAK
003H07	2049456	PAK
003H08	433381	PAK
003H09	879532	PAK
004A01	1566541	PAK
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004A04	45765	PAK
004A05	5735233	PAK
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004A11	4454450	PAK
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004B02	1351731	PAK
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004B09	5223972	PAK
004B12	4544326	PAK
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004C12	1104579	PAK
004D01	751552	PAK
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004D05	5437535	PAK
004D06	5097189	PAK
004D07	5397511	PAK
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004D10	5308284	PAK
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005C10	3642669	PAK
005C11	543492	PAK
005C12	543492	PAK
005D01	1739361	PAK
005D02	4375879	PAK
005D03	2854969	PAK
005D04	3183786	PAK
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005D06	4549325	PAK
005D08	806743	PAK
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005F08	1680865	PAK
005F10	2185333	PAK
005F11	4299947	PAK
005F12	1130487	PAK
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005G03	4422899	PAK

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005G07	5059743	PAK
005G08	1843340	PAK
005G09	6107697	PAK
005G10	4364428	PAK
005G11	4026064	PAK
005G12	1099396	PAK
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005H04	2144520	PAK
005H05	1807286	PAK
005H06	1807286	PAK
005H08	3699645	PAK
005H10	1515737	PAK
005H11	395319	PAK
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006A02	3402303	PAK
006A04	2079699	PAK
006A05	2008375	PAK
006A06	433381	PAK
006A08	3592139	PAK
006A09	3453875	PAK
006A10	794950	PAK
006A11	5819801	PAK
006A12	3468427	PAK
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006B04	3511738	PAK
006B05	4241233	PAK
006B06	2471515	PAK
006B07	2048265	PAK
006B08	2469575	PAK
006B09	696492	PAK
006B10	846315	PAK
006B11	166848	PAK
006B12	4741112	PAK
006C01	433381	PAK
006C02	4064994	PAK
006C03	1280374	PAK
006C04	3596440	PAK
006C05	1442814	PAK
006C07	577497	PAK
006C09	1784068	PAK
006C10	2240534	PAK
006C12	4047002	PAK
006D01	4070007	PAK
006D02	6085314	PAK
006D03	1150463	PAK
006D05	3610871	PAK
006D06	5310625	PAK
006D07	517361	PAK
006D08	2892863	PAK

006D09	3327334	PAK
006D10	2229992	PAK
006D11	1878712	PAK
006D12	3916203	PAK
006E01	147621	PAK
006E02	147622	PAK
006E03	688108	PAK
006E04	688115	PAK
006E06	5023473	PAK
006E11	4844174	PAK
006F03	6230087	PAK
006F06	6257292	PAK
006F07	3086149	PAK
006F10	3020409	PAK
006F11	5211588	PAK
006F12	5211588	PAK
006H03	2264576	PAK
006H05	5597985	PAK
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94049123	metK	Escherichia coli	546
97075927	rpoD	Rhodobacter capsulatus	576
98414051	ygjD	Escherichia coli	580
90330537	surA	Escherichia coli	594
88262245	era	Escherichia coli	771
97295239	era	Salmonella typhimurium	771
97113525	tolQ	Pseudomonas aeruginosa	969
97113525	tolR	Pseudomonas aeruginosa	970
97113525	tolA	Pseudomonas aeruginosa	971
92355498	dapE	Escherichia coli	1162
95095976	flhA	Paracoccus denitrificans	1452
98414051	ycfB	Escherichia coli	1678
98429489	clpP	Caulobacter crescentus	1801
98429489	clpX	Caulobacter crescentus	1802
93224448	lon	Myxococcus xanthus	1803
99065127	lolA	Escherichia coli	2614
94110226	infA	Escherichia coli	2619
98241618	lpxK	Escherichia coli	2981
91348525	metZ	Escherichia coli	3107
92193258	folC	Escherichia coli	3111
96405645	htrB	Escherichia coli	3242
95014035	surE	Escherichia coli	3625
94240115	frr	Escherichia coli	3653
93077430	smbA	Escherichia coli	3654
96228708	ispA	Shigella flexneri	4043
88163790	tufA	Escherichia coli	4265
90264268	rpoB	Escherichia coli	4270
96107188	lpxC	Escherichia coli	4406
84236117	ftsZ	Escherichia coli	4407
84236117	ftsA	Escherichia coli	4408
93003529	murG	Bacillus subtilis	4412
97361813	ftsW	Escherichia coli	4413
99047598	mraY	Escherichia coli	4415
99029898	rluD	Escherichia coli	4544
99000128	obg	Streptomyces coelicolor	4566
97284515	ispB	Escherichia coli	4569
93259941	murl	Escherichia coli	4662
91311678	infB	Escherichia coli	4744
92355498	dnaj	Escherichia coli	4760
92355498	dnak	Escherichia coli	4761
98414051	yjeQ	Escherichia coli	4952
96070892	kdtA	Escherichia coli	4988
96405645	msbA	Escherichia coli	4997
96347399	trxA	Synechocystis	5240
97177775	trxA	Rhodobacter sphaeroides	5240
93125123	polA	Streptococcus pneumoniae	5493
94012475	glmU	Escherichia coli	5552

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